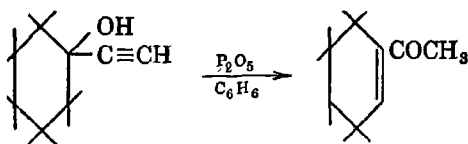


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1-ACETYLCYCLOHEXENE

(Ketone, 1-cyclohexenyl methyl)



Submitted by J. H. SAUNDERS.¹

Checked by E. L. JENNER and R. S. SCHREIBER.

1. Procedure

In a 500-ml. round-bottomed flask are placed 40 g. (0.32 mole) of 1-ethynylcyclohexanol (p. 47), 250 ml. of dry benzene, 10 g. of phosphorus pentoxide, and a boiling chip. A reflux condenser is attached to the flask, and the benzene solution is refluxed gently on a steam cone for 2.5 hours. At the end of that time the contents of the flask are cooled and the benzene is decanted from the phosphorus pentoxide, washed once with 100 ml. of 5% sodium bicarbonate solution, and dried over 15 g. of anhydrous sodium sulfate. The benzene is removed by distillation at atmospheric pressure, and the acetylcyclohexene is carefully fractionated at reduced pressure, through a 15-cm. helix-packed column. The yield of material boiling at 85–88°/22 mm., n_D^{20} 1.4892, is 22.5–28 g. (56–70%).

2. Methods of Preparation

1-Acetylcyclohexene has been prepared by treating cyclohexene with acetyl chloride and aluminum chloride,^{2,3,4,5} by treating 1-ethynylcyclohexanol with oxalic acid⁶ or 85% aqueous

formic acid,^{5,7,8,9} and by the dehydrohalogenation and hydrolysis of ethylenecyclohexane nitrosochloride.¹⁰

¹ This investigation was carried out under the sponsorship of the Office of Rubber Reserve, Reconstruction Finance Corporation, in connection with the Government Synthetic Rubber Program.

² Darzens, *Compt. rend.*, **150**, 707 (1910).

³ Christ and Fuson, *J. Am. Chem. Soc.*, **59**, 895 (1937).

⁴ Nightingale, Milberger, and Tornisek, *J. Org. Chem.*, **13**, 358 (1948).

⁵ Hurd and Christ, *J. Am. Chem. Soc.*, **59**, 120 (1937).

⁶ Levina and Vinogradova, *J. Applied Chem. U.S.S.R.*, **9**, 1299 (1936) [*C.A.*, **31**, 2587 (1937)].

⁷ Rupe, Messner, and Kambli, *Helv. Chim. Acta*, **11**, 454 (1928).

⁸ Fischer and Löwenberg, *Ann.*, **475**, 203 (1929).

⁹ Chanley, *J. Am. Chem. Soc.*, **70**, 246 (1948).

¹⁰ Wallach, *Ann.*, **360**, 46 (1908).

ACRYLIC ACID

I. PYROLYSIS METHOD



Submitted by W. P. RATCHFORD.

Checked by ARTHUR C. COPE, WILLIAM R. ARMSTRONG, and JAMES J. RYAN.

1. Procedure

A 90-cm. length of 28-mm. (outside diameter) Pyrex tubing packed with pieces of Pyrex tubing (Note 1) is mounted vertically in an electric furnace (Note 2) capable of maintaining a temperature of 585–595°. A 250-ml. long-stemmed separatory funnel is connected to the upper end of the tubing with a stopper (Note 3), and the lower end is connected to a 500-ml. three-necked flask immersed in ice water. The flask, which serves as a receiver, is attached to a 50-cm. water-cooled reflux condenser, which in turn is connected by short lengths of rubber tubing to two traps in series which are immersed in a Dry Ice-trichloroethylene mixture. The exit tube of the second trap is vented to a hood. From 0.2 to 0.3 g. of hydroquinone is placed in the

receiver, together with a few pieces of Dry Ice which serve to displace air from the entire apparatus. The third neck of the receiver is stoppered.

The furnace is heated to 590° (Note 4), and after the air has been displaced 200 g. (216 ml., 2 moles) of ethyl acrylate (Note 5) is placed in the separatory funnel and admitted to the reaction tube at a rate of about 90 drops a minute (Note 3), so that the addition requires about 2 hours. At the end of the addition the contents of the receiver and the small amount of liquid in the traps are combined. The total weight of crude acrylic acid containing some ethyl acrylate is 126–136 g.

The crude product is placed in a 250-ml. flask containing a capillary inlet tube through which carbon dioxide is admitted. Ten grams of hydroquinone and 15 g. of diphenyl ether are added, and the flask is attached to a suitable fractionating column (Note 6). The product is fractionated carefully (Note 7) at 135 mm. pressure. The pressure is lowered gradually when most of the ethyl acrylate has distilled, and at about 70°/90 mm. the receiver is changed. The first fraction (mostly ethyl acrylate) amounts to 9–10 g. The pressure is lowered further to 50 mm., and the acrylic acid is distilled fairly rapidly, without reflux, at 69–71°/50 mm. The acrylic acid fraction weighs 108–116 g. and is 95–97% pure according to acidimetric titration. The yield is 68–75% based upon 100% acrylic acid content (Notes 8 and 9).

If the acrylic acid is not to be used at once, it is stabilized by the addition of hydroquinone and is stored in a refrigerator.

2. Notes

1. The middle third of the Pyrex tube should be packed with 20-mm. lengths of fire-polished 7-mm. Pyrex tubing. The lower end of the tube is drawn out to a size that permits attachment to the receiver with a rubber stopper.

2. A type FD303 combustion furnace (made and sold by the Hoskins Manufacturing Company, Detroit, Michigan) or any similar furnace is satisfactory.

3. A groove filed in the stopcock of the separatory funnel aids in controlling the rate of addition. If available, a small constant-

feed pump may be used to introduce the ester into the pyrolysis tube. The rate of addition of the ester is not critical, but at high rates cracking is incomplete and at low rates the yield is reduced. A slow stream of nitrogen (100 bubbles per minute) flowing through the tube reduces refluxing and makes the feed rate easier to observe. The nitrogen may be introduced through a tube in the stopper holding the separatory funnel or through a side arm sealed near the upper end of the pyrolysis tube.

4. The temperature is measured by a movable Chromel-Alumel thermocouple located in the furnace by the side of the tube and connected to a potentiometer or millivoltmeter. The thermocouple junction is adjusted so that during the run it is at the hottest point in the furnace. For the Hoskins Company furnace this point is about 9 in. from the top of the furnace. The temperature is controlled manually to $590 \pm 5^\circ$ by means of an autotransformer (Variac) rated at 5 amperes, 110 volts.

5. Commercial ethyl acrylate, containing hydroquinone inhibitor, may be used directly if it is of good quality.

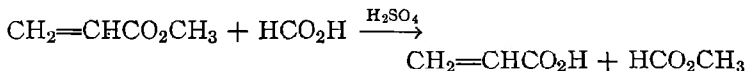
6. The submitter used an insulated column with a 38 by 1.1 cm. section packed with $\frac{1}{8}$ -in. copper helices made of No. 26 B & S gauge copper wire. He states that a column packed with glass helices is unsatisfactory. The checkers used a 100 by 1.7 cm. Vigreux column. Either type of column should be equipped with a total condensation, partial take-off head.

7. Ethyl acrylate and acrylic acid polymerize easily, and overheating must be avoided in the distillation. The flask is heated in an oil bath which is not permitted to rise above 115° . The diphenyl ether which is added serves to expel the acrylic acid at the end of the distillation.

8. The submitter states that the product may be purified by freezing and decanting the supernatant liquid several times. The acrylic acid may be obtained in 97% purity by this method, but it has a faint yellow color. The yield is 50 to 60%.

9. The submitter states that methacrylic acid may be prepared in a similar manner by pyrolyzing ethyl methacrylate. Under the same conditions of temperature and feed rate, the conversion is slightly higher and the yield is about the same.

II. ACIDOLYSIS METHOD



Submitted by C. E. REHBERG.

Checked by ARTHUR C. COPE and ELBERT C. HERRICK.

1. Procedure

One hundred and eighty-four grams (151 ml., 4 moles) of formic acid (Note 1), 1032 g. (1060 ml., 12 moles) of methyl acrylate (Note 2), 30 g. of hydroquinone, and 2 ml. of sulfuric acid are mixed in a 2-l. two-necked round-bottomed flask fitted with a capillary inlet tube. The flask is attached to a 100 by 1.7 cm. Vigreux column (Note 3) and is heated in an oil bath at 85–95°. The mixture is heated under total reflux until the temperature of the vapor at the still head falls to 32° (after 1–3 hours). Methyl formate then is distilled slowly at 32–35° as long as it is formed (8–10 hours). A reflux ratio of about 5 to 1 is maintained during the first part of the distillation, which is decreased to total take-off at the end. When no more methyl formate is produced, the excess methyl acrylate is distilled at 32–35°/140 mm. with the bath temperature at 60–65°. During the distillation, a slow stream of carbon dioxide is admitted through the capillary inlet. When all the methyl acrylate has been removed, the acrylic acid is distilled at 53–56°/25 mm. Upon redistillation through the same column (Note 4) acrylic acid of 97% purity (by acidimetric titration) is obtained in a yield of 220–230 g. (74–78% based upon 100% acrylic acid content), b.p. 54–56°/25 mm.

2. Notes

1. Acetic acid may be used, but it reacts much less rapidly and less completely, and fractionation of the reaction mixture is more difficult. Pure formic acid (98–100%) is preferred.

2. Commercial methyl acrylate may be used without purification if it is of good quality.

3. Either a Vigreux column or a column containing an open

spiral of copper or Nichrome wire is satisfactory. The column should be jacketed and fitted with a total condensation, variable take-off head.

4. Hydroquinone or another polymerization inhibitor should be added before distillation of acrylic acid or its esters.

3. Methods of Preparation

Acrylic acid free of water has been prepared by treating lead acrylate with hydrogen sulfide;^{1,2} by heating α,β dibromopropionic acid with copper;³ by dry distillation of a mixture of equivalent amounts of sodium acrylate and β -chloropropionic acid,⁴ and by the two methods described in these preparations.⁵

¹ Caspary and Tollens, *Ann.*, **167**, 252 (1873).

² Wohlk, *J. prakt. Chem.*, (2) **61**, 212 (1900).

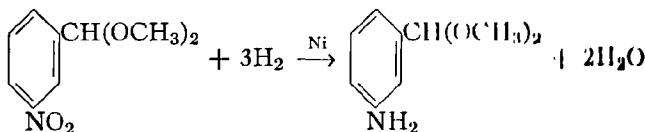
³ Büllmann, *J. prakt. Chem.*, (2) **61**, 491 (1900).

⁴ Rüber and Schetelig, *Z. physik. Chem.*, **48**, 348 (1904).

⁵ Ratchford, Rehberg, and Fisher, *J. Am. Chem. Soc.*, **66**, 1864 (1944).

m-AMINO BENZALDEHYDE DIMETHYLACETAL

(Benzaldehyde, *m*-amino-, dimethylacetal)



Submitted by ROLAND N. ICKE, C. E. REDEMANN, BURNETT B.

WISEGARVER, and GORDON A. ALLES.

Checked by H. R. SNYDER and FRANK X. WERDER

1. Procedure

In a 1-l. steel bomb¹ are placed 295 g. (1.5 moles) of *m*-nitrobenzaldehyde dimethylacetal (p. 72), 250 ml. of technical anhydrous methanol, and 1 tablespoon of Raney nickel catalyst.² Hydrogen is introduced until the pressure is about 1000 lb. (Note 1). The bomb is heated to about 40°, at which point the heating is discontinued and the shaker is started. The by

drogenation soon becomes rapid as the temperature rises to about 70° (Note 2). The bomb is refilled with hydrogen as many times as necessary (Note 3). The theoretical amount of hydrogen (4.5 moles) is absorbed in about 1.5 hours.

The bomb is cooled, the remaining hydrogen is discharged, and the bomb is opened. The solution is transferred to a beaker, and the bomb is rinsed with a little methanol which is added to the solution. The catalyst is removed by filtration (*Caution! The catalyst may be pyrophoric*), and most of the filtrate is transferred to a 500-ml. Claisen flask set on a steam bath for distillation of the methanol; the remainder of the filtrate is introduced into the Claisen flask when the volume of the first portion has been reduced sufficiently by distillation. After all the methanol has been removed the aminoacetal is distilled under diminished pressure. The yield of *m*-aminobenzaldehyde dimethylacetal, a light-yellow liquid boiling at 123–124°/4 mm. or 110–112°/1.5 mm., is 168–196 g. (67–78%).

2. Notes

1. The hydrogenation is similar to one described earlier.¹ As the bomb does not contain enough hydrogen to complete the reduction, more hydrogen should be admitted whenever the pressure drops below 300 lb.

2. Because of the high heat capacity of the bomb the internal temperature continues to rise (to about 70°) after the heater is turned off. As the exothermic hydrogenation begins the temperature rises to about 80°. The temperature should be kept below 85° to prevent hydrogenolysis of the acetal.

3. If the hydrogenation is started at a pressure of about 1500 lb. in a 2.5-l. bomb it will not be necessary to introduce more hydrogen. However, it may be necessary to stop the shaker occasionally to prevent a temperature rise beyond 85°.

3. Methods of Preparation

This acetal has not been described previously. The corresponding diethylacetal has been prepared by the reduction of

m-nitrobenzaldehyde diethylacetal with sodium sulfide¹ and by the reaction of the anhydro compound of *m*-aminobenzaldehyde with ethanolic hydrogen chloride and ethyl orthoformate.⁴

¹ *Org. Syntheses*, **22**, 9 (1942).

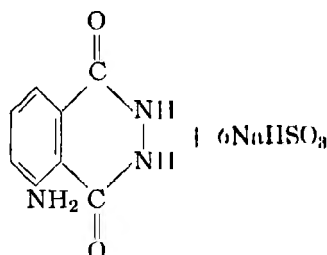
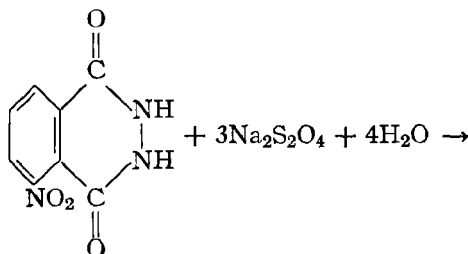
² *Org. Syntheses*, **21**, 15 (1941).

³ Haworth and Lapworth, *J. Chem. Soc.*, **121**, 76 (1922).

⁴ Bottomley, Cocker, and Nanney, *J. Chem. Soc.*, **1937**, 1891.

5-AMINO-2,3-DIHYDRO-1,4-PHTHALAZINEDIONE

(1,4-Phthalazinedione, 5-amino-2,3-dihydro-)



Submitted by CARL T. REDEMANN and C. ERNST REDEMANN.

Checked by CLIFF S. HAMILTON and C. W. WINTER.

1. Procedure

In a 1-l. conical flask are placed 52 g. (about 0.15 mole) of the equimolecular mixture of 5-nitro-2,3-dihydro-1,4-phthalazinedione (p. 78) and sodium sulfate (Note 1), 200 ml. of water, and 75 ml. of 15 *N* ammonium hydroxide solution (sp. gr. 0.90). The flask is stoppered and shaken until all, or very nearly all, of

the solid has dissolved, and 84 g. (0.4 mole) of sodium hydro-sulfite dihydrate (Note 2) is added in three portions. The solution becomes hot, the temperature sometimes reaching the boiling point, and the dark orange-red color begins to fade. After the spontaneous reaction has subsided the solution is boiled gently for a few minutes and filtered to remove any insoluble impurities. The filtrate is heated on a steam bath or over a small flame for 30 minutes. During this time the 5-amino-2,3-dihydro-1,4-phthalazinedione begins to separate as a light-yellow flocculent precipitate or as a crust adhering to the walls of the flask. The hot solution is made distinctly acid to litmus paper with glacial acetic acid and allowed to stand overnight. The yellow precipitate is separated by filtration, washed well with cold water, and dried in a hot-air oven at 110° or below. The dry material weighs 25–27 g. and melts with decomposition at 301–305° (Note 3).

This material is sufficiently pure for most purposes. The chief impurities are small amounts of inorganic salts and a trace of the unreduced nitro compound. If a purer product is desired the crude material (5 g. per 100 ml.) is dissolved in hot 3 *N* hydrochloric acid, decolorizing carbon is added, the solution is filtered promptly (Note 4), and the filtrate is made just faintly acid to Congo red paper with concentrated ammonium hydroxide. After the mixture has cooled to room temperature the pale yellow flocculent precipitate is separated by filtration, washed well with cold water, and dried in the oven at 100° or below. The recovery in the crystallization is 70–75% (Note 5), and the product melts at 329–332° (Note 4).

2. Notes

1. No advantage is gained by using the purified nitro compound.

2. The success of this reduction depends upon the quality of the sodium hydrosulfite. The reagent should be taken from a fresh bottle; material which has stood in the laboratory for a long time probably has undergone oxidation.

3. The submitters used a Kullmann copper block for the

melting-point determinations. The melting point of the pure material has been reported in the literature at various values between 319° and 333°.

4. The 5-amino-2,3-dihydro-1,4-phthalazinedione should not be exposed to the hot hydrochloric acid longer than necessary since some hydrolysis appears to take place.

5. The percentage yield cannot be calculated with precision, since the exact quantity of nitro compound in the mixture taken for the reduction is unknown. The quantity of sodium hydro-sulfite dihydrate employed is sufficient for the reduction of only 0.133 mole of nitro compound; the weight of the purified amino compound corresponds to about 80% of the theoretical yield calculated on the assumption that the hydrosulfite is the limiting reagent.

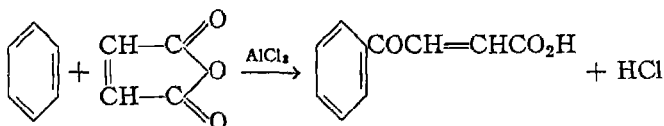
3. Methods of Preparation

5-Amino-2,3-dihydro-1,4-phthalazinedione, also called luminol and 3-aminophthalhydrazide, has been prepared from 5-nitro-2,3-dihydro-1,4-phthalazinedione by reduction with ammonium sulfide¹ or stannous chloride² and by catalytic hydrogenation over palladium on charcoal in alkaline solution³ and by the reaction of 3-aminophthalimide² with hydrazine hydrate.

¹ Huntress, Stanley, and Parker, *J. Am. Chem. Soc.*, **56**, 241 (1934).

² Drew and Pearman, *J. Chem. Soc.*, **1937**, 30.

³ Wegler, *J. prakt. Chem.*, **148**, 135 (1937)

β -BENZOYLACRYLIC ACID(Acrylic acid, β -benzoyl)

Submitted by OLIVER GRUMMITT, E. I. BECKER, and C. MIESSE.

Checked by ARTHUR C. COPE and CLAUDE F. SPENCER.

1. Procedure

In a 1-l. three-necked round-bottomed flask fitted with a mercury-sealed stirrer and a reflux condenser are placed 34 g. (0.347 mole) of maleic anhydride (Note 1) and 175 g. (200 ml., 2.24 moles) of dry, thiophene-free benzene. Stirring is started, and, when the maleic anhydride has dissolved, 100 g. (0.75 mole) of anhydrous reagent grade aluminum chloride powder is added in 6-8 portions through the third neck of the flask at a rate so that the benzene refluxes moderately. The addition requires about 20 minutes. The mixture is then heated under reflux on a steam bath and stirred for 1 hour. The reaction flask is cooled thoroughly in an ice bath, a 250-ml. dropping funnel is attached to the third neck, and the mixture is hydrolyzed by adding 200 ml. of water with stirring and cooling (the first 50 ml. during 15-20 minutes and the balance in about 10 minutes), followed by 50 ml. of concentrated hydrochloric acid (Note 2). Stirring is continued for an additional 40 minutes, during which time it may be necessary to use a spatula to scrape adhering particles of the red-brown aluminum chloride addition compound from the walls of the flask.

The hydrolyzed mixture is transferred to a 1-l. Claisen flask, the transfer of material being completed by rinsing with about 50 ml. of warm water. The flask is heated in a water bath at 50-60°, and the benzene and some water are distilled at 20-30 mm. pressure (Note 3). While the residue is still molten, it is

transferred to a 1-l. beaker, and the flask is rinsed with 50 ml. of warm water. After standing at 0–5° for 1 hour, the yellow solid is collected on a suction filter and washed with a solution of 25 ml. of concentrated hydrochloric acid in 100 ml. of water and then with 100 ml. of water. The washing is done most efficiently by suspending the solid in the wash liquid, cooling to 0–5° with stirring, and then filtering with suction. The preparation should not be interrupted before this point (Note 3), at which stage the crude acid may be air-dried overnight at room temperature if desired. The crude product is dissolved in a solution of 40 g. of anhydrous sodium carbonate in 250 ml. of water by warming to 40–50° (Note 4), 2 g. of Celite or other filter aid is added, and the solution is filtered with suction while warm. After the filter has been washed with two 30-ml. portions of warm water, 2 g. of Norite is added to the combined filtrates and the mixture is heated at 40–50° for 10–15 minutes with frequent stirring, then filtered with suction. The clear, yellow filtrate is transferred to a 1-l. beaker and cooled to 5–10°, and 70 ml. of concentrated hydrochloric acid is added dropwise with stirring. Efficient cooling and stirring are necessary to avoid the precipitation of the acid as an oil. After being cooled to 0–5°, the mixture is filtered with suction; the solid is washed with two 50-ml. portions of cold water and then is dried in the oven at 50° for 12–36 hours to give 56–63 g. of light-yellow anhydrous β -benzoylacrylic acid, m.p. 90–93° (Note 5). The crude acid may be crystallized from benzene, using 12–15 ml. of benzene per 5 g. of acid and cooling at 5–10° (Note 6) to give 44–47 g. of β -benzoylacrylic acid, m.p. 94–96° (Note 7). Concentration of the filtrate to one-fourth to one-fifth of its original volume gives an additional 3–6 g., melting in the range 92–96°. The total yield is 49–52 g. (80–85%).

2. Notes

1. A good grade of commercial maleic anhydride was used, m.p. 52–54°.

2. When β -benzoylacrylic acid is heated with dilute hydrochloric acid, β -benzoyllactic acid is formed, which makes the purification of the product very difficult.¹ For this reason the

mixture is well cooled during hydrolysis and the hydrochloric acid is not added until the heat of the exothermic hydrolysis has been dissipated.

3. The benzene solution of β -benzoylacrylic acid is concentrated under reduced pressure to avoid overheating, and the crude product is separated from aqueous hydrochloric acid without long standing in order to minimize the possibility of forming β -benzoyllactic acid (Note 2).

4. Heating a mixture of β -benzoylacrylic acid and excess sodium carbonate causes hydrolysis to acetophenone and other products, which decreases the yield and interferes with purification of the product.^{2,3}

5. Before drying, the product is the monohydrate, m.p. 64–65° when pure. It is dried until it reaches constant weight and has the melting point of the anhydrous acid.

6. The benzene solution should not be boiled longer than necessary to dissolve the acid, because prolonged heating discolors the product.

7. The evidence indicates that this is the *trans* form of β -benzoylacrylic acid.^{4,5,6} Inhalation of β -benzoylacrylic acid dust should be avoided because of its sternutatory action.

3. Methods of Preparation

β -Benzoylacrylic acid has been prepared by the condensation of acetophenone and chloral to 1,1,1-trichloro-2-hydroxy-3-benzoylpropane, followed by hydrolysis to the corresponding acid and dehydration;⁷ by the action of iodine, potassium iodide, and sodium carbonate on γ -phenylisocrotonic acid;⁸ by bromination of β -benzoylpropionic acid and subsequent dehydrohalogenation;¹ and by the action of phenylzinc chloride on maleic anhydride.⁹ The present method is based on the work of von Pechmann and others.^{2,10,11}

¹ Bougault, *Ann. chim. phys.*, (8) **15**, 491 (1908).

² von Pechmann, *Ber.*, **15**, 885 (1882).

³ Bogert and Ritter, *J. Am. Chem. Soc.*, **47**, 526 (1925).

⁴ Lutz, *J. Am. Chem. Soc.*, **52**, 3405, 3423 (1930).

⁵ Rice, *J. Am. Chem. Soc.*, **52**, 2094 (1930).

⁶ Lutz and Scott, *J. Org. Chem.*, **13**, 284 (1948).

⁷ Koenigs and Wagstaffe, *Ber.*, **26**, 558 (1893).

⁸ Bougault, *Compt. rend.*, **146**, 140 (1908).

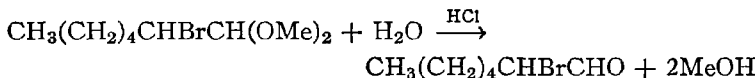
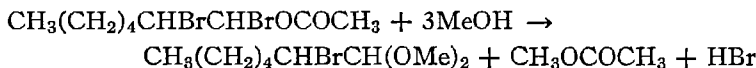
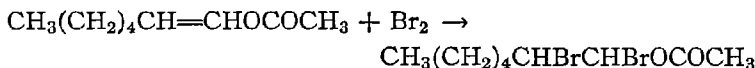
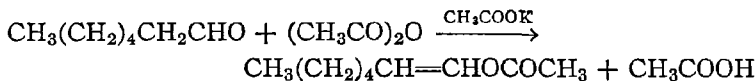
⁹ Tarbell, *J. Am. Chem. Soc.*, **60**, 215 (1938).

¹⁰ Garbriel and Colman, *Ber.*, **32**, 395 (1899).

¹¹ Oddy, *J. Am. Chem. Soc.*, **45**, 2156 (1923).

α -BROMOHEPTALDEHYDE

(Enanthaldehyde, α -bromo-)



Submitted by PAUL Z. BEDOUKIAN.

Checked by JOSEPH A. PAPPALARDO and CHARLES C. PRICE.

1. Procedure

Caution! Since most of the reactants are of unpleasant odor or have lachrymatory effects it is best to use a good hood.

A. Heptaldehyde enol acetate. A mixture of 285 g. (335 ml., 2.5 moles) of heptaldehyde (Note 1), 612 g. (566 ml., 6 moles) of acetic anhydride, and 49 g. (0.5 mole) of powdered potassium acetate is placed in a 2-l. flask fitted with a reflux condenser. The flask is heated in an oil bath kept at 155–160° for 1 hour. The mixture is then allowed to cool, placed in a 2-l. separatory funnel, washed several times with warm water (Note 2) to remove the excess acetic anhydride, and finally washed with 5% sodium carbonate solution (Note 3). The resultant oil is fractionated under reduced pressure through an efficient column

(Note 4). The initial fraction consists of pure heptaldehyde followed by heptaldehyde containing heptaldehyde enol acetate. The fraction boiling at $88-90^{\circ}/17$ mm. is pure enol acetate, n_D^{25} 1.4295–1.4305; d_4^{25} 0.880–0.884. The yield is 175–195 g. (45–50%) (Note 5).

B. *α -Bromoheptaldehyde dimethyl acetal*. A solution of 156 g. (177 ml., 1 mole) of the enol acetate and 200 ml. of carbon tetrachloride is placed in a 1-l. flask and cooled in an ice-water bath. A mixture of 160 g. (51 ml., 1 mole) of bromine and 50 ml. of carbon tetrachloride is added slowly through a buret, the flask being constantly shaken and the rate of addition so controlled as not to allow the temperature of the brominated mixture to rise above 10° (Note 6). The addition of bromine takes from 20 minutes to 1 hour, and the end point is reached when the calculated amount is absorbed and the bromine is no longer decolorized. The brominated mixture is added to 600 ml. of anhydrous methanol (Note 7) and allowed to stand for 48 hours or longer. At the end of this period the mixture is diluted with 2 l. of water and the separated oil (lower layer) is washed with 1 l. of water and finally with 1 l. of 5% sodium carbonate (Note 8). The carbon tetrachloride and methyl acetate are removed by distillation at atmospheric pressure. The residual oil is then distilled under reduced pressure in the presence of a small amount of sodium carbonate. The fraction boiling at $117-119^{\circ}/17$ mm. is collected as pure α -bromoheptaldehyde dimethyl acetal, n_D^{25} 1.4510–1.4520; d_4^{25} 1.180–1.195. The yield is 191–203 g. (80–85%) (Note 9).

C. *α -Bromoheptaldehyde*. A mixture of 119.5 g. (100 ml., 0.5 mole) of α -bromoheptaldehyde dimethyl acetal and 80 ml. of concentrated hydrochloric acid is boiled gently in a 250-ml. distilling flask, and the methanol liberated is removed by distillation, which is continued slowly until the vapor temperature reaches 90° , at which point the heating is stopped and the residue and distillate are combined and diluted with 200 ml. of water. The somewhat brownish oil which separates is distilled under reduced pressure from a 250-ml. Claisen flask. The yield of pure α -bromoheptaldehyde, boiling at $87-92^{\circ}/17$ mm., n_D^{25} 1.4580–1.4600, d_4^{25} 1.210–1.230, is 87–92.5 g. (90–95%).

2. Notes

1. The heptaldehyde should be a freshly distilled product boiling at 151.5–153.5°.

2. Decomposition of the excess acetic anhydride takes place very slowly and with difficulty unless warm water is used. The checkers used three portions of wash water at 40–50°, totaling 1.3 l.

3. The checkers found that five or six portions of 5% sodium carbonate totaling 5.1 were required before rapid carbon dioxide evolution ceased.

4. The reaction mixture consists of unchanged heptaldehyde, heptaldehyde enol acetate, heptaldehyde diacetate, and a small amount of polymerized material. The proportion of free heptaldehyde and heptaldehyde diacetate depends upon the time of heating, longer periods of heating favoring the formation of the diacetate. An efficient fractionating column, preferably of the Whitmore-Fenske type, should be used in order to obtain the enol acetate free of the heptaldehyde and heptaldehyde diacetate impurities. The checkers used a Whitmore-Fenske type column of about six theoretical plates.

5. The residue consists largely of heptaldehyde diacetate, which when slowly distilled at atmospheric pressure partially decomposes to acetic anhydride and heptaldehyde. In this manner, 50–60% of the available heptaldehyde is recovered from the residue.

6. The checkers recommend a mechanical stirrer to avoid danger of contact with bromine.

7. Commercial methanol (99.5–100%) was used in all experiments.

8. The acetal must be free of acid; otherwise decomposition takes place during distillation.

9. The pure bromoacetal is a stable, colorless liquid, of mild odor. It may be kept indefinitely when stored in a dark bottle over a small amount of anhydrous sodium carbonate.

3. Methods of Preparation

The procedure described is an example of a general method of preparation of α -bromoaldehydes.¹ α -Bromoheptaldehyde has been prepared by the bromination of heptaldehyde diethyl acetal with phosphorus trichlorodibromide ² and by direct bromination of heptaldehyde trimer with subsequent treatment with alcohol.³

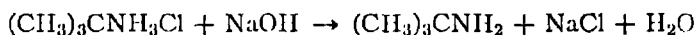
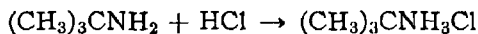
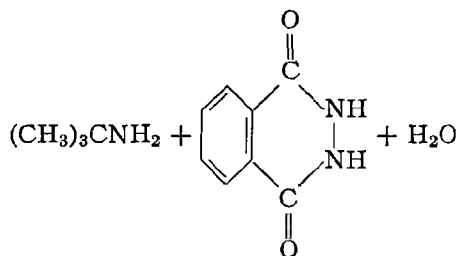
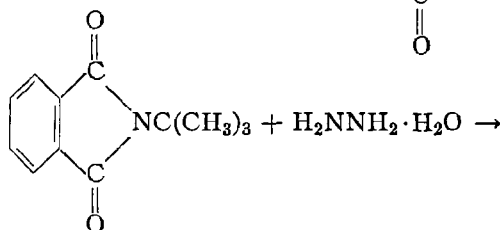
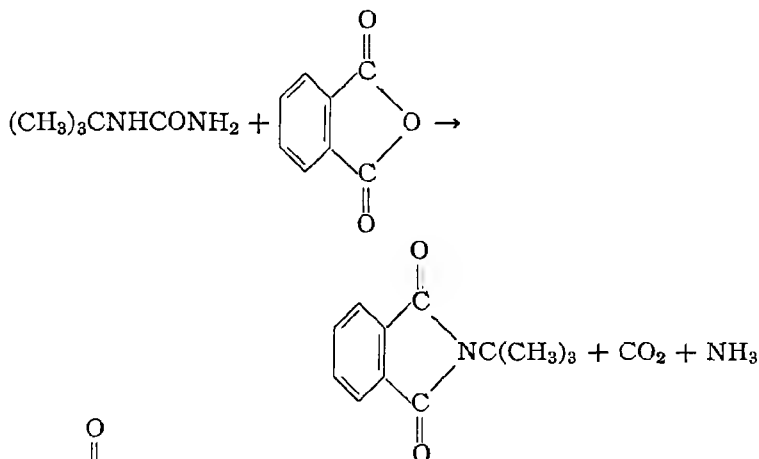
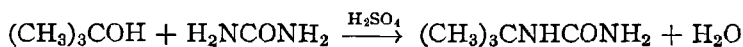
¹ Bedoukian, *J. Am. Chem. Soc.*, **66**, 7 (1944).

² Kirmann, *Compt. rend.*, **184**, 525 (1927); *Ann. chim.*, (10) **11**, 223 (1929).

³ Dworzak and Piffierling, *Monatsh.*, **48**, 251 (1927).

***tert.*-BUTYLAMINE and *tert.*-BUTYLAMINE
HYDROCHLORIDE**

I. VIA *tert.*-BUTYLPHthalIMIDE



Submitted by LEE IRVIN SMITH and OLIVER H. EMERSON,¹
Checked by R. L. SHRIENER and ARNE LANGSJOEN.

1. Procedure

A. *tert.*-Butylurea (Note 1). In a 500-ml. three-necked flask equipped with a fast mechanical stirrer, a 200-ml. dropping funnel, and a thermometer is placed 193 g. (105 ml., 1.98 moles) of concentrated sulfuric acid (sp. gr. 1.84). The flask is surrounded by an ice bath, and 60 g. (1 mole) of finely powdered urea is added slowly at such a rate that the temperature remains between 20° and 25°. Then 148 g. (188 ml., 2 moles) of *tert.*-butyl alcohol is added dropwise from the funnel at such a rate that the temperature is maintained between 20° and 25° (Note 2). After the addition is completed the mixture is stirred for an additional half-hour, allowed to stand at room temperature overnight (about 16 hours) (Note 3), and then poured with stirring on 1.5 kg. of cracked ice and water in a 4-l. beaker. Without removal of the precipitate, the mixture is made alkaline to Congo red indicator by adding slowly with stirring a solution of sodium hydroxide (160 g. in 750 ml. of water). The mixture is cooled with an ice bath to keep the temperature below 25°. The mixture is stirred in the ice bath until the temperature falls to about 15° (Note 4), at which point the precipitate is collected on a 15-cm. Büchner funnel, washed with two 100-ml. portions of cold water, and pressed and sucked as dry as possible. The cake is transferred to a 2-l. beaker, and 500 ml. of water is added. The mixture is heated to boiling and quickly filtered while hot through an 8-cm. steam-heated Büchner funnel (Note 5) with the aid of suction. The filtrate is cooled to 0–5° with occasional stirring, and the white precipitate of *tert.*-butylurea is collected on a 15-cm. Büchner funnel with suction and pressed as dry as possible. After the product has been spread out on absorbent paper and air-dried overnight (Note 6) there is obtained 36–39 g. (31–33%) of *tert.*-butylurea melting at 180–182° (Note 7).

B. *tert.*-Butylphthalimide. Thirty-five grams (0.3 mole) of *tert.*-butylurea and 100 g. (0.675 mole) of phthalic anhydride are ground together in a mortar. The mixture is placed in a 1-l. Erlenmeyer flask which is then immersed in a metal bath previously heated to 200°. The mixture melts and effervesces vigorously; after 10 minutes the temperature of the bath is

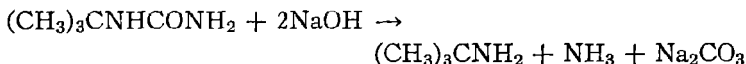
raised to 240° (internal temperature 220°) and held there for 5 minutes (Note 8). The flask is removed and cooled to 60–70°, and 100 ml. of 95% ethanol is added to dissolve the contents partially. A 20% solution of sodium carbonate is added until the solution is alkaline to litmus paper, and the mixture is diluted with water to 1 l. The solid is collected on a Büchner funnel with the aid of suction and pressed as dry as possible. The filter cake is warmed on a steam bath with 500 ml. of petroleum ether (b.p. 60–70°) in a 1-l. flask, and the hot mixture is filtered. Any water layer that may separate from the filtrate is removed, and the filtrate is cooled to 25° and again filtered. The clear filtrate is concentrated by distillation to about one-third of its original volume and placed in a refrigerator overnight. The crystalline material is collected on a filter, and as much as possible of the solvent is removed by suction. After air drying, this first crop weighs 40–43 g. and melts at 58–59°. By concentration of the filtrate an additional 2–4 g. may be obtained. The total yield of *tert*.-butylphthalimide is 43–46.5 g. (72–76%).

C. tert.-Butylamine hydrochloride. In a 2-l. flask fitted with an efficient bulb-type reflux condenser are placed 203 g. (1 mole) of *tert*.-butylphthalimide, 1 l. of 95% ethanol, and 59 g. (1 mole) of 85% hydrazine hydrate. The solution is refluxed for 2 hours and cooled, and concentrated hydrochloric acid (about 100 ml.) is added until the solution is strongly acid to Congo red paper, though a large excess of acid is avoided. The voluminous precipitate of phthalhydrazide is collected on a 15-cm. Büchner funnel with the aid of suction and washed with four 100-ml. portions of 95% ethanol. The combined filtrate and washings are concentrated under reduced pressure to a volume of 200 ml. About 1 l. of water is added, any insoluble material is removed by filtration, and the filtrate is concentrated to about 300–350 ml. If any additional insoluble material separates it is removed by filtration, and the solvent is completely removed by evaporation under reduced pressure. This crude amine hydrochloride may be converted to the free amine as described below or it may be purified by solution in 500 ml. of absolute alcohol, the solution being filtered and 500 ml. of dry ether being added to the filtrate. The crude amine hydrochloride is collected on a filter; the solvent

is removed by suction, and the residue is dissolved in hot absolute ethanol using 5 ml. per gram of material; absolute ether (50% of the volume of ethanol) is added, and the solution is cooled in a refrigerator for several hours. All the *tert.*-butylamine hydrochloride is collected on a Büchner funnel and dried in a vacuum desiccator. It weighs 79–97 g. (72–88%) and melts with sublimation at 270–290°.

D. *tert.*-Butylamine. To 150 ml. of cold 40% solution of sodium hydroxide is added 109.5 g. (1 mole) of *tert.*-butylamine hydrochloride with stirring. The solution is saturated with potassium carbonate (about 100–150 g.); the layer of amine is separated and dried over 20 g. of sodium hydroxide pellets. The product is distilled using an ice-cooled receiver, and the fraction boiling at 44–46° is collected. If the purified amine hydrochloride is the starting material for this step the yield ranges from 65 g. to 69 g. (89–94%). When the crude amine salt is employed, the yield is 46–60 g. (64–83%) (Note 9).

II. HYDROLYSIS OF *tert.*-BUTYLUREA



Submitted by D. E. PEARSON, J. F. BAXTER, and K. N. CARTER.
Checked by R. L. SHRINER and CALVIN N. WOLF.

1. Procedure

A 1-l. round-bottomed flask is charged with 60 g. (1.5 moles) of sodium hydroxide pellets dissolved in 75 ml. of water, 70 g. (0.6 mole) of *tert.*-butylurea, and 225 ml. of commercial ethylene glycol. The flask is fitted with an efficient reflux condenser, and a glass tube is led from the top of the condenser to a small flask immersed in ice water (Note 10).

The mixture is refluxed gently for 4 hours (Note 11). The flask is cooled and equipped for distillation, and the fraction boiling at 40–60° is collected in an ice-cooled receiver. The crude amine, including any collected in the trap, weighs 37–39 g. It is dried overnight with 5–7 g. of sodium hydroxide pellets

(Note 12) and then distilled, a 12 to 15-cm. fractionating column (Note 13) and an ice-cooled receiver equipped with a soda-lime tube being used. The fraction boiling at 44–46° amounts to 31–34 g. (71–78%) of *tert.*-butylamine; d_4^{20} 0.699; n_D^{20} 1.3800.

2. Notes

1. This step may be omitted if a practical grade of *tert.*-butylurea is purchased from the Eastman Kodak Company. Since the commercial product may contain sodium sulfate and di-*tert.*-butylurea it should be recrystallized from hot water, about 1 l. of solvent being used for 100 g. of the urea.

2. The temperature of the mixture should be kept in the range 20–25°. Higher temperatures lead to the formation of diisobutylene, and at lower temperatures (15°) the urea does not dissolve readily. Even at 25° the urea is usually not completely in solution. It has been found convenient to warm the *tert.*-butyl alcohol to about 30–35° before placing it in the dropping funnel. This avoids solidification in the stem (the melting point of *tert.*-butyl alcohol is 25.5°).

3. Longer standing does not improve the yield.

4. If the temperature is allowed to fall below 15°, large amounts of sodium sulfate decahydrate crystallize with the product. If this happens it may be necessary to recrystallize the *tert.*-butylurea several times.

5. The insoluble residue weighs 10–22 g. and consists of di-*tert.*-butylurea which sublimes above 200° but melts in a sealed tube at 243°. If several runs are being made, the di-*tert.*-butylurea should be saved and dried. It may be converted to *tert.*-butylphthalimide in 63% yields by heating with four equivalents of phthalic anhydride under the same conditions as specified for mono-*tert.*-butylurea.

6. The product should not be dried in an oven at elevated temperatures, as it sublimes.

7. This material is pure enough for the next step. Melting points of 172° (dec.) and 183° are given in the literature.^{2,3} Recrystallization from dilute ethanol gives long, white needles melting at 182° (cor.), whereas use of 95% ethanol gives plates

melting at the same temperature. The temperature of the melting-point bath should be raised more rapidly than usual since the product sublimes slowly above 100°.

8. Less rapid heating results in a diminished yield. The reaction is usually completed after a total time of 15 minutes, no further evolution of carbon dioxide or ammonia occurring. Prolonged heating causes the formation of a colored product and reduces the yield.

9. A similar series of reactions may be used to prepare *tert.*-amylamine. The *tert.*-amylurea is produced in yields of 50–58%, *tert.*-amylphthalimide in yields of 63–72%, and *tert.*-amylamine, b.p. 77–78°, in 87% yields (N. L. Drake and John Garman, private communication).

10. If the water in the condenser is cold enough to prevent loss of the amine the extra trap is unnecessary.

11. The *tert.*-butylurea gradually dissolves, and a gelatinous mass of sodium carbonate forms.

12. If an aqueous layer forms it is separated and the amine is dried with a fresh portion of 5 g. of sodium hydroxide pellets.

13. The submitters and checkers used a Vigreux column.

3. Methods of Preparation

tert.-Butylurea has been prepared by the action of *tert.*-butyl bromide upon a mixture of urea and white lead;² by the action of *tert.*-butylamine upon potassium cyanate;³ in small amounts, by heating *N-tert.*-butylurethan with alcoholic ammonia.² The method given above is a modification of a general method for preparation of alkyl ureas, described by Harvey and Caplan in a patent.⁴

tert.-Butylphthalimide is a new compound. The procedure given here is based upon a general procedure for conversion of alkyl ureas to phthalimides, as described by Manske.⁵

In addition to the methods cited under the preparation of *tert.*-butylamine by hydrogenolysis of 2,2-dimethylethyl-eneimine⁶ its formation from trimethylacetamide and trimethylacetazide⁷ should be mentioned. The preparation of *tert.*-

butylamine via *tert.*-butylphthalimide is a modification ⁸ of a general procedure for the cleavage of alkylphthalimides to amines described by Ing and Manske.⁹ The alkaline hydrolysis of *tert.*-butylurea has been published.¹⁰

¹ Work done under a contract with the Office of Scientific Research and Development.

² Schneegans, *Arch. Pharm.*, **231**, 677 (1893).

³ Brander, *Rec. trav. chim.*, **37**, 67 (1917).

⁴ Harvey and Caplan, U. S. pat. 2,247,495 [C.A., **35**, 6267 (1941)].

⁵ Manske, *J. Am. Chem. Soc.*, **51**, 1209 (1929); Tingle and Brenton, *J. Am. Chem. Soc.*, **32**, 116 (1910).

⁶ *Org. Syntheses*, **27**, 12 (1947).

⁷ Bühler and Fierz-David, *Helv. Chim. Acta*, **26**, 2135 (1943).

⁸ Smith and Emerson, *J. Am. Chem. Soc.*, **67**, 1862 (1945).

⁹ Ing and Manske, *J. Chem. Soc.*, **1926**, 2348.

¹⁰ Pearson, Baxter, and Carter, *J. Am. Chem. Soc.*, **70**, 2290 (1948).

CATALYST, RANEY NICKEL

(With High Contents of Aluminum and Adsorbed Hydrogen)



Submitted by HARRY R. BILICA and HOMER ADKINS.

Checked by ARTHUR C. COPE and HAROLD R. NACE.

Caution: The Raney nickel catalysts described below cannot be used safely under all conditions of temperature, pressure, and ratio of catalyst to hydrogen acceptor which are employed with less active nickel catalysts. They are particularly effective for low-pressure hydrogenations. No difficulty has been encountered in their use at temperatures below 100°, or above 100° if the ratio of catalyst to possible hydrogen acceptor is 5% or less. Outside these limits their use sometimes has led to reactions proceeding with violence. In one case a hydrogenation proceeding at 125° and 5000 lb. showed a pressure rise to considerably more than 10,000 lb. before the reaction could be stopped or the pressure released. Several instances of sudden increases in pressure have been noted when 10-15 g. of catalyst was used with a similar amount of hydrogen acceptor in

100 ml. of ethanol in the temperature range of 100–150° under 5000 lb. of hydrogen in a bomb of 270 ml. void. Accordingly the catalysts should be used with caution for high-pressure hydrogenations.

1. Procedure

W-6 Raney nickel catalyst. In a 2-l. Erlenmeyer flask equipped with a thermometer and a stainless-steel stirrer are placed 600 ml. of distilled water and 160 g. of c.p. sodium hydroxide pellets. The solution is stirred rapidly and allowed to cool to 50° in an ice bath equipped with an overflow siphon. Then 125 g. of Raney nickel-aluminum alloy powder is added in small portions during a period of 25–30 minutes. The temperature is maintained at $50 \pm 2^\circ$ by controlling the rate of addition of the alloy to the sodium hydroxide solution and the addition of ice to the cooling bath. When all the alloy has been added, the suspension is digested at $50 \pm 2^\circ$ for 50 minutes with gentle stirring. It is usually necessary to remove the ice bath and replace it with a hot-water bath to keep the temperature constant. After this period of digestion the catalyst is washed with three 1-l. portions of distilled water by decantation (Note 1).

A glass test tube approximately 5.1 cm. in diameter and 38 cm. in length with a side arm sealed 6 cm. from the top is used as the container for washing the catalyst. The tube is closed with a rubber stopper clamped or wired in place tightly enough to withstand a gas pressure of 0.5 atmosphere. The stopper contains three holes through which extend: (1) a tube 10 mm. in diameter reaching to the bottom of the test tube, for admitting distilled water; (2) a T-tube for equalizing gas pressures; (3) a gas-tight bushing through which the $\frac{1}{4}$ -in. shaft of a stainless-steel stirrer projects to the bottom of the washing tube. A 5-l. aspirator bottle containing distilled water is so placed that water will flow from it through a stopcock to the bottom of the washing tube. The side arm of the test tube is connected by pressure tubing to a 5-l. aspirator bottle that serves as an overflow from which the water may be allowed to flow through a stopcock to a drain. A source of distilled water is connected to the reservoir. Other connections and the general arrangement of the apparatus

are shown in Fig. 1, and details of the construction of the gas-tight brass bushing are given in Fig. 2. Rubber pressure tubing and stoppers used in making the connections should be boiled with 5% sodium hydroxide and rinsed with water to remove

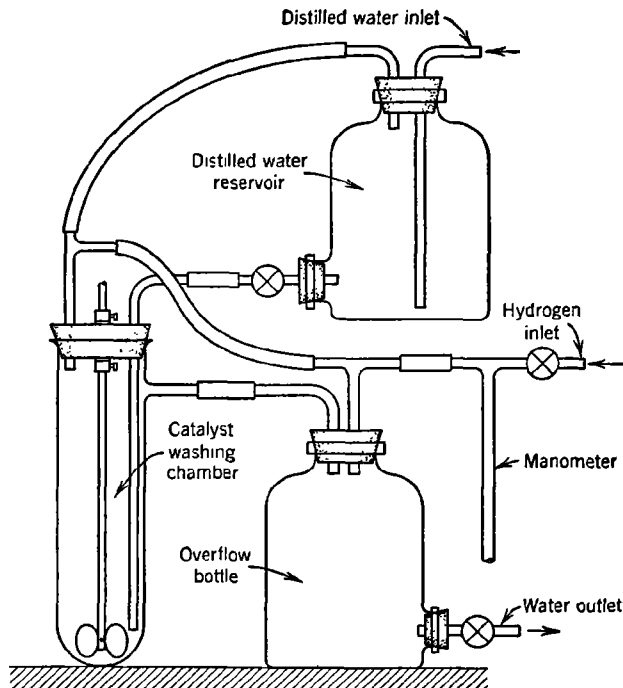


FIG. 1. Apparatus for washing catalyst. It is more convenient to have the inlet tube for wash water sealed into the bottom of the chamber rather than introduced through the stopper as shown.

sulfur. All connections should be wired in place to withstand a pressure of 0.5 atmosphere (7.5 lb.).

The catalyst sludge is transferred to the washing tube immediately after its third washing by decantation. The last portions are rinsed from the flask into the washing tube with distilled water, and the tube, reservoir, and overflow bottle are nearly filled with distilled water. The apparatus is assembled rapidly, and hydrogen is introduced through the inlet while most of the water in the overflow bottle is displaced through the outlet.

The outlet then is closed, and hydrogen is admitted until the water in the reservoir, washing tube, and overflow bottle is under a pressure about 0.5 atmosphere above that of the outside atmosphere. The stirrer is operated at such a speed that the catalyst is suspended to a height of 18–20 cm. Distilled water from the reservoir is allowed to flow through the suspended catalyst at a rate of about 250 ml. per minute. When the reservoir is nearly empty and the overflow bottle full, the drain cock and distilled-water inlet are opened simultaneously to an equal rate of flow such that, as the overflow bottle empties, the reservoir is filled, while the pressure in the system remains constant.

After about 15 l. of water has passed through the catalyst, the stirrer and the flow of water are stopped, the pressure is released, and the apparatus disassembled. The water is decanted from the settled sludge, which is then transferred to a 250-ml. centrifuge bottle with 95% ethanol. The catalyst is washed three times by stirring, not shaking, with 150-ml. portions of 95% ethanol, each addition being followed by centrifuging. In the same manner, the catalyst is washed three times with absolute ethanol. One to two minutes' centrifugation at 1500–2000 r.p.m. is sufficient to separate the catalyst. All operations should be carried out as rapidly as possible if a catalyst of

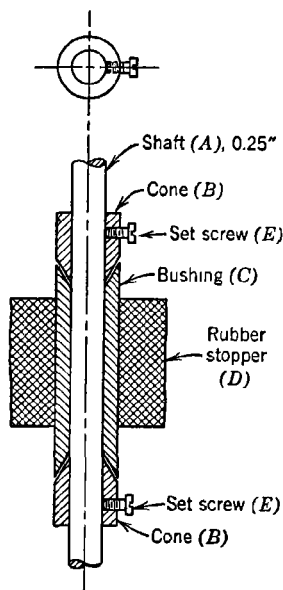


FIG. 2. Gas-tight brass bushing. The gas-tight bushing for the shaft of the stirrer consists of three parts: two cones (B) which fit the shaft snugly and are attached to it by set screws (E); and a bushing (C) so cut that the cones fit into it at top and bottom. The two cones are placed on shaft (A) of the stirrer, above and below the bushing and attached to the shaft so that they fit snugly against the bushing. A gas-tight seal is obtained by placing a drop or two of heavy lubricating oil between each cone and the bushing. The over-all dimensions of the bushing are approximately 13 by 65 mm., and it is held in a rubber stopper (D).

the maximum activity is desired. The catalyst should be kept in a closed bottle filled with absolute ethanol and should be stored at once in a refrigerator. The total elapsed time from the beginning of the addition of the alloy to the completion of the preparation should be not more than about 3 hours (Notes 2, 3, and 4).

2. Notes

1. The procedure in the preparation of W-7 Raney nickel, after the digestion and the three decantations, is to transfer the catalyst to a 250-ml. centrifuge bottle with 95% ethanol. It is then washed three times by stirring, not shaking, with 150-ml. portions of 95% ethanol, with centrifuging after each addition. In the same manner, the catalyst is washed three times with absolute ethanol and is at once stored in a refrigerator in a closed bottle filled with absolute ethanol. The catalyst so prepared contains alkali. This may be advantageous for various reasons in the hydrogenation of ketones, phenols, and nitriles. In certain cases the alkali may have a harmful effect upon a hydrogenation.

2. The volume of the settled catalyst (W-6) in ethanol is about 75–80 ml. containing about 62 g. of nickel and 7–8 g. of aluminum. The catalyst is extremely pyrophoric when exposed to the air in a dry condition, and it should be kept wet with solvent at all times. It amounts to about 28 "half teaspoonfuls" if it is so measured. The catalyst loses some of its special activity upon standing but seems to be quite active for about 2 weeks when stored in a refrigerator. After this period it is similar in activity to the Raney nickel made by an earlier procedure.¹ The W-3 to W-7 catalysts all lose their special activity rather rapidly when stored under water.

3. A somewhat less active but nevertheless excellent catalyst, referred to as W-5, is made by the procedure described above for W-6 except that it is washed at atmospheric pressure without the addition of hydrogen to the system. The W-5 catalyst is similar in method of preparation and activity to the W-4 Raney nickel catalyst as prepared by Pavlic.²

4. Raney nickel, prepared by the procedure described for W-6, will bring about the hydrogenation of alkyne and alkene

linkages, of aldehydes, ketones, oximes, nitriles, nitro compounds, and benzenoid and pyridinoid nuclei under the conditions of temperature and pressure normally employed with platinum and palladium catalysts.³ At higher pressures W-6 Raney nickel brings about reactions at a more rapid rate and at lower temperatures than Raney nickel prepared by the older procedures.

3. Methods of Preparation

The various procedures for the preparation of Raney nickel⁴ from the nickel-aluminum alloy differ from one another in the method of adding the alloy, in the concentration of sodium hydroxide, in the temperature and duration of digestion, and in the method of washing the catalyst free of sodium aluminate and alkali. For convenience in reference, the Raney nickel catalysts prepared by various procedures have been designated W-1,⁵ W-2,¹ W-3,^{2,6} W-4,^{2,6} W-5,³ W-6,³ and W-7.³ They have been compared as to activity against β -naphthol.⁷ A Raney nickel catalyst is available commercially from the Gilman Paint and Varnish Company, Chattanooga, Tennessee.

¹ *Org. Syntheses*, **21**, 15 (1941).

² Pavlic and Adkins, *J. Am. Chem. Soc.*, **68**, 1471 (1946).

³ Adkins and Billica, *J. Am. Chem. Soc.*, **70**, 695 (1948).

⁴ Murray Raney, U. S. pat. 1,628,190 [*C.A.*, **21**, 2116 (1927)].

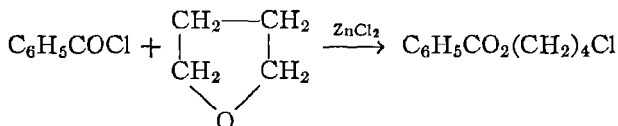
⁵ Covert and Adkins, *J. Am. Chem. Soc.*, **54**, 4116 (1932).

⁶ Adkins and Pavlic, *J. Am. Chem. Soc.*, **69**, 3039 (1947).

⁷ Adkins and Krsek, *J. Am. Chem. Soc.*, **70**, 412 (1948).

4-CHLOROBUTYL BENZOATE

(1-Butanol, 4-chloro-, benzoate)



Submitted by MARTIN E. SYNERHOLM.

Checked by ARTHUR C. COPE and JAMES J. RYAN.

1. Procedure

In a 200-ml. round-bottomed flask fitted with an efficient reflux condenser are mixed 31.4 ml. (38 g., 0.27 mole) of freshly distilled benzoyl chloride, 28.2 ml. (25 g., 0.35 mole) of tetrahydrofuran (Note 1), and 5 g. of freshly fused zinc chloride. A vigorous reaction begins immediately, and after a few seconds, when the mixture starts to boil, external cooling is applied with an ice bath. After the initial reaction has subsided, the mixture is heated on a steam bath for 15 minutes, cooled, and dissolved in 100 ml. of benzene. The benzene solution is washed with 100 ml. of a 5% solution of sodium chloride and then with 100 ml. of a saturated solution of sodium bicarbonate. The benzene layer is dried over anhydrous sodium sulfate and fractionally distilled from a modified Claisen flask.

The product is collected at 140–143°/5 mm., 132–135°/2.5 mm.; n_D^{25} 1.5176 (Note 2). The yield is 45–48 g. (78–83%).

2. Notes

1. Good-quality commercial tetrahydrofuran may be used as received, or redistilled; b.p. 65–66°.

2. The product develops a slight yellow tint on standing.

3. Methods of Preparation

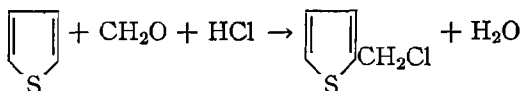
4-Chlorobutyl benzoate has been prepared by the action of benzoyl chloride on tetrahydrofuran in the presence of titanium chloride, stannic chloride,¹ or zinc chloride.²

¹ Gol'dfarb and Smorgonskii, *J. Gen. Chem. U.S.S.R.*, **8**, 1516 (1938) [*C.A.*, **33**, 4593 (1939)].

² Cloke and Pilgrim, *J. Am. Chem. Soc.*, **61**, 2667 (1939).

2-CHLOROMETHYLTHIOPHENE

(Thiophene, 2-chloromethyl-)



Submitted by K. B. WIBERG and H. F. McSIANE.

Checked by CLIFF S. HAMILTON and J. L. PAULEY.

1. Procedure

Caution! The procedure should be carried out under a hood since the product is lachrymatory.

In a 2-l. beaker surrounded by an ice-salt bath (Note 1), and fitted with a mechanical stirrer and a thermometer, are placed 420 g. (392 ml., 5 moles) of thiophene (Note 2) and 200 ml. of concentrated hydrochloric acid. A rapid stream of hydrogen chloride (Note 3) is passed continuously into the mixture with vigorous stirring. When the temperature reaches 0°, 500 ml. of 37% formaldehyde solution (Note 4) is added at a rate that will permit the temperature to remain below 5°. The addition requires about 4 hours. When all the formaldehyde solution has been added, the mixture is extracted with three 500-ml. portions of ether. The ether extracts are combined, washed successively with water and saturated sodium bicarbonate solution, and then dried over anhydrous calcium chloride.

The solvent is removed by distillation, and the product is distilled under reduced pressure through a 50-cm. fractionating column (Note 5). The product boiling at 73–75°/17 mm. is collected. The yield is 257–267 g. (40–41%) of a colorless oily liquid (Note 6).

2. Notes

1. The checkers preferred to use a Dry Ice bath or to add Dry Ice to the reaction mixture as needed.

2. The thiophene used by the submitters was that supplied by the Socony-Vacuum Oil Company. It was used without any additional purification.

3. A satisfactory hydrogen chloride generator has been described earlier.¹

4. The apparatus should be set up in a hood, for, although nearly all the hydrogen chloride is absorbed, a small amount does escape. The rate of addition of hydrogen chloride should be such that nearly complete absorption is maintained at all times.

According to the submitters paraformaldehyde (165 g., 5.5 moles) may be substituted for the formaldehyde solution. This modification affords an easier control of the temperature. However, paraformaldehyde does not react to any appreciable extent below 0°, and so the temperature should be kept between 0° and 5°. The reaction time is 6–8 hours, and the yield is unchanged.

5. A Vigreux column was used by both the submitters and checkers.

6. Some *bis*(2-thienyl)methane may be obtained from the residue at 125–126°/9 mm. When recrystallized from methanol it melts at 46–47°.

It is advisable not to store the chloromethylthiophene for any length of time, as it has a tendency to decompose. However, if it is to be stored, it is best kept cold, and in the dark. If the product is to be used for the preparation of 2-thiophenaldehyde, it is convenient to convert it to the stable hexamethylenetetrammonium salt, for storage.

3. Methods of Preparation

2-Chloromethylthiophene has been prepared by the action of hydrogen chloride on 2-thienylcarbinol² and by the action of hydrogen chloride and formaldehyde on thiophene.³ The above procedure is essentially that of Blicke and Burckhalter.³

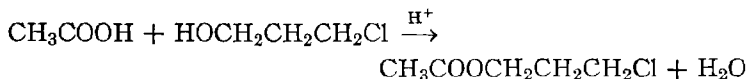
¹ *Org. Syntheses*, Coll. Vol. 1, 534 (1941).

² Biedermann, *Ber.*, 19, 636 (1886).

³ Blicke and Burckhalter, *J. Am. Chem. Soc.*, 64, 477 (1942).

γ -CHLOROPROPYL ACETATE

(1-Propanol, 3-chloro-, acetate)



Submitted by C. F. H. ALLEN and F. W. SPANGLER.

Checked by MILLARD SEELEY and C. R. NOLLER.

1. Procedure

A 1-l. round-bottomed flask is fitted with a 30-cm. Vigreux column (Note 1) connected to a condenser. The condenser leads to an automatic separator arranged so that the lighter liquid is returned to the flask.¹ In the flask is placed a mixture of 189 g. (167 ml., 2 moles) of trimethylene chlorohydrin,² 180 g. (172 ml., 3 moles) of glacial acetic acid, 300 ml. of benzene, and 2 g. of *p*-toluenesulfonic acid monohydrate. The mixture is refluxed at such a rate that the temperature at the top of the column remains at 69° (boiling point of benzene-water azeotrope) during the time the greatest amount of water is distilling, and rises gradually to 80° (boiling point of benzene-acetic acid azeotrope) as the last of the water is removed. The volume of the aqueous layer collected varies with the temperature of the vapors and the length of time required for distillation, but it is approximately

50 ml. at the end of the reaction; the time required is 7-9 hours (Note 2).

The solution is cooled, then washed successively with two 500-ml. portions of 10% sodium carbonate solution, one 500-ml. portion of water, and one 100-ml. portion of saturated sodium chloride solution. The wash solutions are extracted successively with one 100-ml. portion of benzene, which is added to the main benzene solution. After removal of the benzene the ester is distilled at atmospheric pressure through a 30-cm. asbestos-wrapped Vigreux column, the fraction boiling at 166-170°, n_D^{22} 1.4295, being collected. The yield of colorless product is 257-260 g. (93-95%).

2. Notes

1. The submitters prefer to use the Clarke-Rahrs ester column,³ for which they claim two distinct advantages: (1) dehydration requires no attention beyond occasionally noting the amount of distillate—when no more aqueous layer separates the reaction is over; (2) reagents do not need to be dry—any water present is removed during the heating.

2. Titration of an aliquot portion of the aqueous layer with standard alkali will give the amount of acetic acid carried over, from which the amount of water can be determined. The expected amount of water is 36 ml.

3. Methods of Preparation

γ -Chloropropyl acetate has been prepared by heating 1-bromo-3-chloropropane and potassium acetate in glacial acetic acid,⁴ and by the action of acetyl chloride on trimethylene chlorohydrin.^{5,6}

¹ *Org. Syntheses* Coll. Vol. 1, 422 (1941).

² *Org. Syntheses* Coll. Vol. 1, 533 (1941).

³ *Synthetic Org. Chemicals*, Vol. IX, No. 3, Eastman Kodak Company, May, 1936.

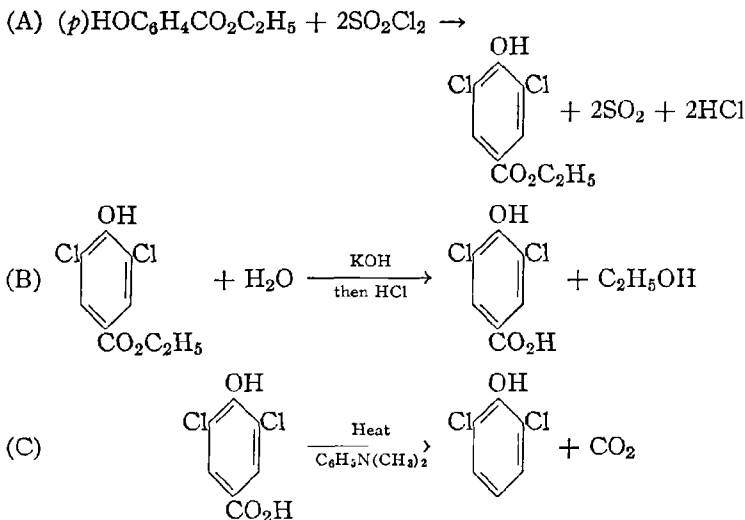
⁴ Henry, *Bull. acad. roy. Belg.*, **1900**, 738 [*C.A.*, **1**, 1969 (1907)]

⁵ Derick and Bissel, *J. Am. Chem. Soc.*, **38**, 2483 (1916).

⁶ Lespieau, *Bull. soc. chim. France*, **7**, 254 (1940).

2,6-DICHLOROPHENOL

(Phenol, 2,6-dichloro-)



Submitted by D. S. TARBELL, J. W. WILSON, and PAUL E. FANTA.
 Checked by R. L. SHRINER and ARNE LANGSJOEN.

1. Procedure

A. *Ethyl 3,5-dichloro-4-hydroxybenzoate*. A tared 2-l. round-bottomed flask is equipped with an efficient reflux condenser connected through a calcium chloride drying tube to a gas-absorption trap, and is set up on a steam bath in a hood. In the flask are placed 250 g. (1.5 moles) of ethyl 4-hydroxybenzoate (Note 1) and 444 g. (266 ml., 3.3 moles) of sulfuryl chloride. The mixture is warmed on the steam bath (gently at first) until gas is no longer evolved (about 1 hour). Then 50 ml. of sulfuryl chloride is added to the reaction flask, and the warming is continued until gas is no longer evolved. This entire chlorination procedure requires about 1.5 hours. The excess sulfuryl chloride is then removed by attaching a water pump through an empty

safety flask to the reaction flask and warming on the steam bath until no evidence of vapor can be detected above the white solid in the reaction flask. The residue in the flask should weigh about 350 grams (Note 2). Recrystallization from a mixture of 600 ml. of ethanol and 140 ml. of water gives 315–334 g. (83–88%) of ethyl 3,5-dichloro-4-hydroxybenzoate hydrate (Note 3) melting at 110–114° with decomposition.

B. *3,5-Dichloro-4-hydroxybenzoic acid*. In a 2-l. round-bottomed flask equipped with a reflux condenser and set upon a steam bath are placed 315 g. (1.25 moles) of ethyl 3,5-dichloro-4-hydroxybenzoate hydrate and 600 ml. of Claisen's alkali (Note 4). Saponification is brought to completion by heating on the steam bath for 1 hour. A yellow homogeneous solution results which is diluted with 400 ml. of water and acidified to Congo red paper by pouring it into a rapidly stirred solution of 320 ml. of concentrated hydrochloric acid and 380 ml. of water in a 4-l. beaker. The thick white slurry is then cooled to 0–10°; the acid is collected on a 20-cm. Büchner funnel and washed with two 250-ml. portions of cold water (Note 5). After being freed from as much water as possible by suction, the filter cake is broken up and dissolved in a boiling mixture of 1 l. of ethanol and 350 ml. of water. Cooling to 0° gives the first crop of crystals, weighing about 200 g. Concentration of the mother liquors to 750 ml. and cooling to 0° yields an additional 40–50 g. of product of equal purity. After drying in an oven at 85–95° for 8 hours, the white crystalline acid weighs 240–250 g. (93–97%) and melts at 266–268°.

C. *2,6-Dichlorophenol*. A mixture of 250 g. (1.2 moles) of dry 3,5-dichloro-4-hydroxybenzoic acid and 575 g. (600 ml., 4.8 moles) of redistilled dimethylaniline is placed in a 2-l. round-bottomed flask provided with a thermometer and a short air-cooled condenser and is heated slowly in an oil bath. Evolution of gas commences at 130° and is vigorous at 150°. The solution is heated at 190–200° for 2 hours or until the evolution of gas has ceased. After cooling, the solution is poured by portions into 600 ml. of concentrated hydrochloric acid in a 3-l. separatory funnel, with cooling from time to time by holding the funnel under a stream of cold water. When the solution is

thoroughly cooled and acid to Congo red paper, the phenol is extracted with three 250-ml. portions and three 100-ml. portions of ether (Note 6). The combined ether extracts are washed with 15 ml. of 6 *N* hydrochloric acid, dried overnight over 20 g. of anhydrous sodium sulfate, and filtered into a 2-l. Claisen flask, and the ether is removed by distillation. After cooling, the residue begins to solidify, and 500 ml. of petroleum ether (40–60°) is added. After the phenol has been brought into solution by refluxing gently on the steam bath it is poured into a 1-l. beaker and cooled to 0°. A crop of white crystals (130–140 g.) is collected, having a melting point of 64.5–65.5°. By concentration of the mother liquor to 200 ml., a second crop (25–40 g.) melting at 64–65° can be collected. The total yield amounts to 157–180 g. (80–91%) (Note 7).

2. Notes

1. The ethyl 4-hydroxybenzoate was obtained from the Eastman Kodak Company and melted at 115.5–116°.

2. If the product weighs much less than 350 g. at this point, an additional 50 ml. of sulfuryl chloride should be added and the heating continued until gas is no longer evolved.

3. The ester crystallizes from dilute alcohol as the monohydrate; after long drying in a vacuum desiccator over phosphorus pentoxide, it melts at 111–112°.

4. Claisen's alkali is prepared by dissolving 350 g. of potassium hydroxide in 250 ml. of water, cooling, and diluting to 1 l. with methyl alcohol.

5. If the acid is dried completely at this point it contains about 5% potassium chloride. The submitters state that recrystallization is unnecessary if the acid is to be used in Part C.

6. The aqueous layer should be saved. Low yields are due to incomplete extraction of the 2,6-dichlorophenol. If the final yield is low, the aqueous layer should be extracted with three 100-ml. portions of ether and the product recovered by following the procedure outlined.

7. If the product is colored or low melting it may be purified further by recrystallization from 600 ml. of petroleum ether

(40–60°) containing about 4 g. of Norite. By cooling and concentrating, 170–175 g. may be recovered (m.p. 65–66°) from 180 g. of crude product.

3. Methods of Preparation

2,6-Dichlorophenol has been prepared by the chlorination of phenol with chlorine gas in the presence of nitrobenzene and fuming sulfuric acid,¹ by the decomposition of the diazotate of 2,6-dichloro-4-aminophenol,² and by the decarboxylation of 3,5-dichloro-4-hydroxybenzoic acid in quinoline³ or dimethylaniline.⁴

¹ Huston and Neeley, *J. Am. Chem. Soc.*, **57**, 2177 (1935).

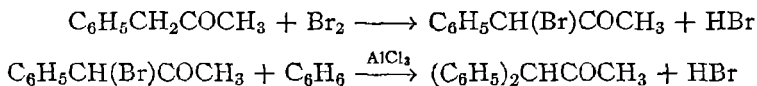
² Seifart, *Ann., Spl.*, **7**, 203 (1870).

³ Blicke, Smith, and Powers, *J. Am. Chem. Soc.*, **54**, 1467 (1932).

⁴ Tarbell and Wilson, *J. Am. Chem. Soc.*, **64**, 1066 (1942).

α,α -DIPHENYLACETONE

(2-Propanone, 1,1-diphenyl-)



Submitted by EVERETT M. SCHULTZ and SALLY MICKEY.

Checked by EDWARD T. CLINE and R. S. SCHREIBER.

1. Procedure

A. α -Bromo- α -phenylacetone. A 1-l. three-necked flask is equipped with a sealed stirrer (Note 1), a dropping funnel, and a water-cooled reflux condenser provided with a short inverted U tube on the open end; the equipment is assembled in the hood. In the flask are placed 200 ml. of dry, thiophene-free benzene (Note 2) and 37 g. (36.89 ml., 0.276 mole) of phenylacetone (Note 3). The stirrer is started, and 45 g. (14.42 ml., 0.28 mole) of reagent bromine is added dropwise during a period of 1 hour. The reaction mixture first becomes cloudy but changes to a clear

orange-red solution by the time all the bromine is added. After the addition of bromine is complete, a rapid stream of dry nitrogen or carbon dioxide is passed through the solution by means of an inlet tube which now replaces the dropping funnel. The hydrogen bromide issuing from the inverted U tube at the top of the condenser may be trapped in water in an Erlenmeyer flask or other container adjusted so that the water surface is about 1 cm. below the outlet of the tube. The reaction is complete when no more hydrogen bromide fumes can be detected in the gas issuing from the condenser. This operation requires 3-6 hours. During this period the reaction mixture becomes yellow to green in color. The benzene solution of α -bromo- α -phenylacetone is then transferred to a dry 500-ml. separatory funnel (Note 4).

B. α,α -Diphenylacetone (Note 5). The reaction flask used in A is again equipped as it was originally, and in it are placed 75 g. (0.56 mole) of anhydrous aluminum chloride (Note 6) and 150 ml. of dry benzene (Note 2). The stirrer is started, and the flask is heated by means of a steam bath so that the benzene boils gently. The benzene solution of α -bromo- α -phenylacetone (Part A) is added dropwise from the separatory funnel to the boiling mixture over a period of 1 hour. After the addition is complete, the almost black reaction mixture is heated to boiling for an additional hour, then cooled and poured with stirring onto 500 g. of crushed ice and 100 ml. of concentrated hydrochloric acid contained in a 2-l. beaker. The deeply colored benzene solution gradually becomes orange-yellow. When the ice has melted, the benzene layer is separated and the aqueous layer is extracted with three 50-ml. portions of ether. The combined ether and benzene solution is washed with 100 ml. of water and then with 100 ml. of saturated sodium bicarbonate solution. After the solution has been dried for at least 1 hour over 60 g. of anhydrous sodium sulfate, the solvents are evaporated on a steam bath until the solution no longer boils. The dark residue is transferred to a 250-ml. Claisen flask equipped for reduced-pressure distillation and having a receiver fused to the side arm (Note 7). The residual benzene is first distilled at 19-20 mm. while the flask is being heated on a steam bath. The steam bath

is replaced by an oil or metal bath which is gradually heated to 190°. A small fore-run of yellow oil which darkens rapidly is collected. It is removed from the receiver by siphoning and rinsing with acetone. The bath is allowed to cool to 100–120°, the system is evacuated with an oil pump (Note 8), and the diphenylacetone is distilled. The bulk of the material boils at 142–148°/2–3 mm. The distillate may solidify in the receiver (Note 9). The crude product is triturated with just sufficient petroleum ether (b.p. 35–60°) to moisten it, cooled in an ice-water bath, collected on a filter, and washed on the filter with small amounts of petroleum ether at 0–5° until nearly colorless. The amount of petroleum ether used up to this point should not exceed 50 ml. The product is then crystallized from petroleum ether using 8 ml. of solvent per gram of crude, dry solid. The hot solution is allowed to stand at room temperature until crystallization begins, and then at 0–5° for 16 hours (Note 10). The crystals are collected by filtration and dried in air at room temperature. The yield of nearly colorless product melting at 60–61° (Note 11) is 31–33 g. (53–57%).

2. Notes

1. A rubber tubing seal is satisfactory. The submitters used an all-glass seal made from a 5-ml. glass syringe.

2. The benzene was reagent grade and was dried by distilling until no more water collected in the condenser. The undistilled portion was used directly.

3. Phenylacetone was obtained from the Swope Oil Company, Philadelphia, Pennsylvania. On attempted distillation of this material as received, the checkers observed considerable water in the fore-run. The distillation was interrupted, the material was dried over anhydrous sodium sulfate and redistilled at atmospheric pressure, but small amounts of water still appeared in the condensate, indicating possible decomposition. The fraction boiling at 214–214.8° (uncor.)/756 mm. was used.

4. The transfer may be carried out easily by admitting dry nitrogen or air under pressure continuously to the flask and allowing the benzene solution to be blown out of the flask through

the glass tube previously used for introducing nitrogen or carbon dioxide.

5. Once Part B is started, it should be continued without interruption until the Friedel-Crafts reaction product is decomposed.

6. Baker and Adamson reagent grade powdered aluminum chloride was used.

7. Diphenylacetone may solidify in the side arm, in which event it may become necessary to melt it by heating with a small flame.

8. It is necessary to protect the pump by means of a sodium hydroxide tower since hydrogen halide may be evolved during the distillation. The checkers, in addition, used a Dry Ice trap.

9. The checkers transferred the distillate to another container before solidification occurred.

10. The checkers found that the small additional amount (approximately 5 g.) of product obtained by cooling to -25° is more highly colored and considerably less pure than that obtained at $0-5^{\circ}$.

11. A labile form of α,α -diphenylacetone, melting at 46° , is described in the literature.^{1,2}

3. Methods of Preparation

α,α -Diphenylacetone has been prepared by the oxidation of 1,1-diphenyl-2-propanol;¹ by the action of dilute mineral acid on 1,1-diphenyl-1,2-propanediol,^{1,2} 1,1-diphenyl-1-hydroxy-2-ethoxypropane,³ 1,1-diphenyl-1-hydroxy-2-aminopropane,⁴ 1,1-diphenyl-2-ethoxy-1-propene,⁵ and 2,2-diphenyl-3-methylethylenimine;⁶ by the distillation at atmospheric pressure of 1,1-diphenyl-2-methylethylene oxide;⁷ and by the reaction of benzene with α -phenyl- α -chloro- (or bromo-) acetone.⁸ The present method is adapted from the procedure of Ruggli, Dahn, and Wegmann.⁸

¹ Tiffeneau and Dorlencourt, *Compt. rend.*, **143**, 127 (1906).

² Stoermer, *Ber.*, **39**, 2302 (1906); Tiffeneau and Levy, *Bull. soc. chim. France*, **83**, 776 (1923).

³ Stoermer, *Ber.*, **39**, 2302 (1906).

⁴ Thomas and Bettziechi, *Z. physiol. Chem.*, **140**, 265 (1924).

⁵ Bardan, *Bull. soc. chim. France*, **49**, 1875 (1931).

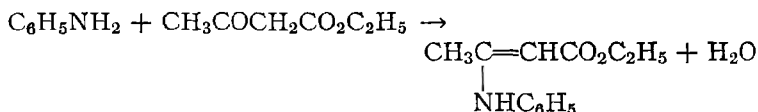
⁶ Campbell, McKenna, and Chaput, *J. Org. Chem.*, **8**, 107 (1943).

⁷ Levy and Lagrave, *Compt. rend.*, **180**, 1032 (1925); *Ann. chim.*, (10) **8**, 365 (1927).

⁸ Richard, *Compt. rend.*, **200**, 753 (1935); Ruggli, Dahn, and Wegmann, *Helv. Chim. Acta*, **29**, 113 (1946).

ETHYL β -ANILINOCROTONATE

(Crotonic acid, β -anilino-, ethyl ester)



Submitted by GEORGE A. REYNOLDS and CHARLES R. HAUSER.

Checked by ARTHUR C. COPE and WILLIAM R. ARMSTRONG.

1. Procedure

In a 1-l. round-bottomed flask attached to a Dean and Stark constant water separator (Note 1) which is connected to a reflux condenser are placed 46.5 g. (45.5 ml., 0.5 mole) of redistilled aniline, 65 g. (63.5 ml., 0.5 mole) of commercial ethyl acetoacetate, 100 ml. of benzene, and 1 ml. of glacial acetic acid. The flask is heated in an oil bath at about 125°, and the water which distils out of the mixture with the refluxing benzene is removed at intervals. Refluxing is continued until no more water separates (9 ml. collects in about 3 hours) and then for an additional 30 minutes. The benzene is then distilled under reduced pressure, and the residue is transferred to a 125-ml. modified Claisen flask with an insulated column. The flask is heated in an oil or metal bath maintained at a temperature not higher than 120° while the fore-run of aniline and ethyl acetoacetate is removed by distillation under reduced pressure, and at 140–160° during distillation of the product (Note 2). The yield of ethyl β -anilinocrotonate boiling at 128–130°/2 mm., n_D^{25} 1.5770, is 78.82 g. (76.80%).

2. Notes

1. A Dean and Stark separator made with a stopcock for removal of water¹ or any continuous water separator which will return the benzene to the reaction mixture may be used.

2. The submitters state that if the temperature of the bath rises much above 120° during distillation of the fore-run, or much above 160° during distillation of the product, the ethyl β -anilinocrotonate may be contaminated with diphenyl urea, part of which may precipitate from the distillate on standing. Such a precipitate can be removed by adding an equal volume of 30–60° petroleum ether to the distillate and filtering. The petroleum ether is distilled from the filtrate, and the residue is placed in a vacuum desiccator over mineral oil or is redistilled.

3. Methods of Preparation

The procedure described is a modification of procedures employed previously. Ethyl β -anilinocrotonate is obtained when the reactants are allowed to stand at room temperature for several days without a catalyst,^{2,3,4} or are heated on a steam bath,⁴ or are allowed to stand for 12 hours in the presence of a catalytic amount of aniline hydrochloride.⁵ Iodine also is a catalyst.⁵ Properties of the ester are reported by Coffey, Thomson, and Wilson.⁵

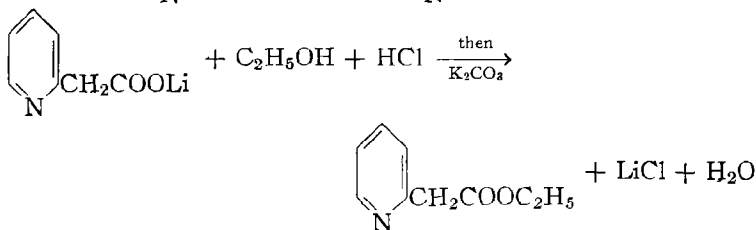
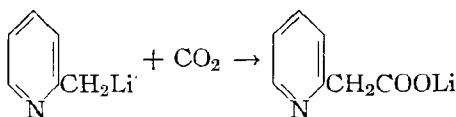
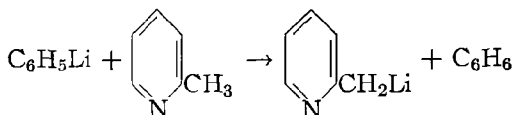
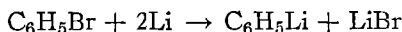
¹ Cope, Hofmann, Wyckoff, and Hardenbergh, *J. Am. Chem. Soc.*, **63**, 3452 (1941).

² Knorr, *Ber.*, **16**, 2593 (1883).

³ Limpach, *Ber.*, **64**, 969 (1931).

⁴ Conrad and Limpach, *Ber.*, **20**, 944 (1887).

⁵ Coffey, Thomson, and Wilson, *J. Chem. Soc.*, **1936**, 856.

ETHYL 2-PYRIDYLACETATE**(2-Pyridineacetic acid, ethyl ester)**

Submitted by R. B. WOODWARD and E. C. KORNFIELD.

Checked by ARTHUR C. COPE and WILLIAM R. ARMSTRONG.

1. Procedure

A 2-l. round-bottomed three-necked flask is fitted with a reflux condenser, a dropping funnel, and an efficient mechanical stirrer. A calcium chloride tube is attached to the condenser to protect the apparatus from moisture. To the flask are added 800 ml. of absolute ether and 13.9 g. (2 gram atoms) of lithium chips or shavings (Note 1). The stirrer is started, and 105 ml. (157 g., 1 mole) of dry bromobenzene is placed in the dropping funnel. About 5-15 ml. of the bromobenzene is added to initiate the reaction; when the ether begins to reflux, the balance is added at such a rate that the solvent refluxes continuously (1 hour) (Note 2). The mixture is then stirred and refluxed until most of the lithium disappears (15-90 min.). While stirring is con-

tinued, 97 ml. (93.1 g., 1 mole) of α -picoline is added dropwise in about 5–10 minutes. The dark red-brown solution of picolyl-lithium is stirred for an additional 30 minutes and is then poured slowly and with shaking onto 500–750 g. of crushed Dry Ice contained in a 3-l. round-bottomed flask (Note 3). The mixture is stirred well until the dark color of the picolyl-lithium is discharged, and the excess of Dry Ice is allowed to evaporate. The ether is removed by distillation under reduced pressure at room temperature. The lumpy residue of lithium salts is broken up, and to it is added 750 ml. of commercial absolute ethanol. The solution is saturated with dry hydrogen chloride while cooling in an ice bath. The esterification mixture is allowed to stand overnight, after which the solvent is removed as completely as possible by distillation under reduced pressure on a steam bath. The syrupy residue is dissolved in 750 ml. of chloroform, and a paste prepared from 225 g. of potassium carbonate and 135 ml. of water is slowly added to the solution with mechanical stirring. After the paste has been added, the solution is stirred vigorously and is kept just below the boiling point for 1 hour. The chloroform solution is decanted from the inorganic salts, and the chloroform is removed by distillation. The residue is fractionated under reduced pressure from a modified Claisen flask with a fractionating side arm. About 40 g. of α -picoline is recovered in the fore-run, and the ethyl 2-pyridyl-acetate is obtained as a light yellow liquid, b.p. 135–137°/28 mm., 142–144°/40 mm., 109–112°/6 mm.; n_D^{25} 1.4979. The yield is 58–66 g. (35–40% based on lithium) (Notes 4 and 5).

2. Notes

1. The most convenient method of preparing the lithium chips is as follows: Pieces of lithium several grams each in size and slightly moist with paraffin oil are pounded with a hammer into thin sheets on a dry surface. The sheets are quickly cut into small chips by means of a pair of scissors and are added immediately to the absolute ether.

2. The use of a nitrogen atmosphere is not essential if the solution is kept protected from oxygen by an atmosphere of

ether vapor. For this purpose the solution is kept at the reflux point throughout.¹

3. Rapid filtration of the picolylithium solution onto the Dry Ice through a thin layer of glass wool is useful in removing unreacted lithium at this point.

4. Runs twice the size of the one described give comparable yields.

5. Methyl 2-pyridylacetate, b.p. 122–125°/21 mm., can be obtained in similar yield by use of methanol in the esterification.

3. Methods of Preparation

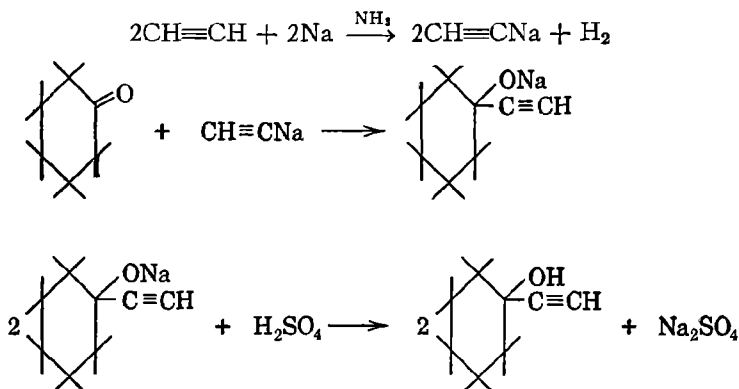
2-Pyridylacetic esters have been obtained previously only by the method of Oparina,² through alcoholysis of 2-pyridylacetanilide which was obtained by Beckmann rearrangement of the oxime of 2-phenacylpyridine.

¹ *Org. Syntheses*, **23**, 83 (1943).

² Oparina and Smirnov, *Khim. Farm. Prom.*, **1934**, No. 4, 15 [*C.A.*, **29**, 1820 (1935)]; *J. Gen. Chem. U.S.S.R.*, **5**, 1699 (1935) [*C.A.*, **30**, 2567 (1936)].

1-ETHYNYLCYCLOHEXANOL

(Cyclohexanol, 1-ethynyl-)

Submitted by J. H. SAUNDERS.¹

Checked by R. S. SCHREIBER and E. L. JENNER.

1. Procedure

A rapid stream of dry acetylene is passed into approximately 1 l. of liquid ammonia in a 2-l. three-necked flask equipped with a gas inlet tube and a mechanical stirrer while 23 g. (1 gram atom) of sodium is added over a period of 30 minutes (Notes 1 and 2). The flow of acetylene is then reduced (Note 3), and 98 g. (1 mole) of cyclohexanone is added dropwise. When this addition, which requires about an hour, is completed, the reaction mixture is allowed to stand for about 20 hours to permit the evaporation of nearly all the ammonia (Note 4).

The solid residue is decomposed by adding approximately 400 ml. of ice and water, and the resulting mixture is carefully acidified with 50% sulfuric acid (Note 5). The organic layer is dissolved in 100 ml. of ether and washed with 50 ml. of brine. The original aqueous phase and the brine wash are then extracted with two 50-ml. portions of ether. The combined ethereal

solutions are dried over anhydrous magnesium sulfate and filtered, and the ether is distilled. The product is then distilled under reduced pressure through a good column (Note 6). The yield of 1-ethynylcyclohexanol is 81–93 g. (65–75%), b.p. 74°/14 mm.; n_D^{20} 1.4822 (Note 7).

2. Notes

1. The preparation of sodium acetylide is based on the procedure of Vaughn, Hennion, Vøgt, and Nieuwland.²

2. The blue color of dissolved sodium is discharged so rapidly by the acetylene that it seldom spreads through the entire mixture.

3. The flow of acetylene may be terminated before the cyclohexanone is added. This operation, however, is alleged to increase the formation of glycol.³

4. If all the ammonia is allowed to evaporate and the residual solid is exposed to the air the yields may be decreased.

5. Upwards of 70 ml. is required. The amount depends upon the quantity of ammonia remaining.

6. The submitters and the checkers used a 15-cm. Vigreux column.

7. The product may solidify to a colorless solid, m.p. 30°.

3. Methods of Preparation

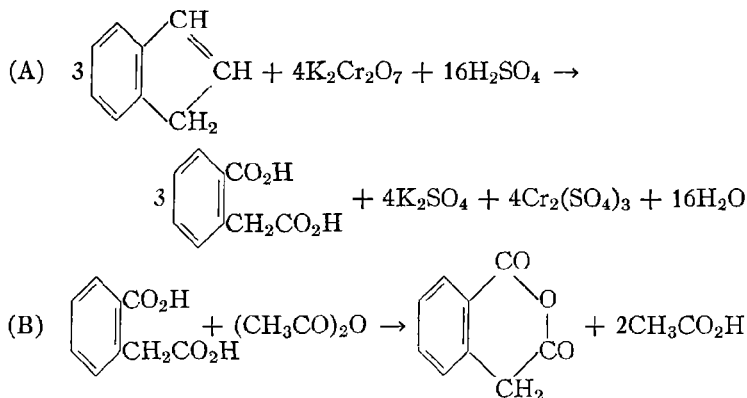
An attractive alternative procedure for the preparation of 1-ethynylcyclohexanol which gives yields of 80–90% employs the potassium salt of *tert.*-amyl alcohol to effect the addition of acetylene to cyclohexanone.^{4, 5, 6} This condensation has been brought about by a suspension of sodium amide in ether^{7, 8, 9, 10, 11} and by potassium hydroxide in ether.¹² 1-Ethynylcyclohexanol has also been prepared by the action of acetylene on the sodium enolate of cyclohexanone.¹³ The procedure described here is essentially that of Campbell, Campbell, and Eby.^{3, 14}

¹ This investigation was carried out under the sponsorship of the Office of Rubber Reserve, Reconstruction Finance Corporation, in connection with the Government Synthetic Rubber Program.

- ² Vaughn, Hennion, Vogt, and Nieuwland, *J. Org. Chem.*, **2**, 1 (1937).
³ Campbell, Campbell, and Eby, *J. Am. Chem. Soc.*, **60**, 2882 (1938).
⁴ Pinkney, Nesty, Wiley, and Marvel, *J. Am. Chem. Soc.*, **58**, 972 (1936).
⁵ Dimroth, *Ber.*, **71B**, 1333 (1938).
⁶ Backer and van der Bij, *Rec. trav. chim.*, **62**, 561 (1943).
⁷ Ger. pat. 289,800 [*Frdl.*, **12**, 55 (1914-1916)].
⁸ Locquin and Sung, *Bull. soc. chim. France*, **35**, 597 (1924).
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¹⁰ Levina and Vinogradova, *J. Applied Chem. U.S.S.R.*, **9**, 1299 (1936) [*C.A.*, **31**, 2587 (1937)].
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¹² Azerbaev, *J. Gen. Chem. U.S.S.R.*, **15**, 415 (1945) [*C.A.*, **40**, 4683 (1946)].
¹³ Hurd and Jones, *J. Am. Chem. Soc.*, **56**, 1924 (1934).
¹⁴ Chanley, *J. Am. Chem. Soc.*, **70**, 244 (1948).

HOMOPHTHALIC ACID AND ANHYDRIDE

(α-Toluic acid, o-carboxy-, and 2-benzopyran-1,3-dione)



Submitted by OLIVER GRUMMITT, RICHARD EGAN, and ALLEN BUCK.
 Checked by R. L. SHRINER and WALTER R. KNOX.

1. Procedure

A. Homophthalic acid. A solution of 243 g. (0.83 mole) of technical potassium dichromate in 3.6 l. of water and 1330 g. (725 ml., 13 moles) of concentrated sulfuric acid is prepared in a 5-l. three-necked flask fitted with a sealed mechanical stirrer, a thermometer, a 100-ml. dropping funnel, and a reflux condenser.

The mixture is warmed to 65° , and 72 g. (72 ml., 0.56 mole) of technical 90% indene (Note 1) is added dropwise from the dropping funnel. The temperature must be kept at $65 \pm 2^{\circ}$, and cooling by a water bath is necessary during the addition. After the addition is complete the mixture is stirred for 2 hours at $65 \pm 2^{\circ}$ (Note 2). At the end of this period the mixture is cooled with stirring to $20-25^{\circ}$ and then further cooled in an ice-salt bath for 5 hours at 0° . The homophthalic acid which separates is collected on a 10-cm. Büchner funnel with the aid of suction, then washed with two 75-ml. portions of ice-cold 1% sulfuric acid and once with 75 ml. of ice water (Note 3). The precipitate is then dissolved in 215 ml. of 10% sodium hydroxide solution, and the resulting solution is extracted with two 50-ml. portions of benzene (Note 4), which are discarded. The aqueous solution is added to 160 ml. of 33% sulfuric acid with vigorous stirring, and the mixture is chilled in an ice-salt bath for 2-3 hours. The homophthalic acid is collected on a 10-cm. Büchner funnel with the aid of suction, washed with three 25-ml. portions of ice water, and pressed and sucked as dry as possible. The acid is transferred to a 500-ml. distilling flask, 300 ml. of benzene is added, and the mixture is distilled from a steam bath until about 250 ml. of distillate (benzene and water) has been collected (Note 5). The slurry of acid and benzene is filtered with the aid of suction through a 10-cm. Büchner funnel, and the product is spread out on a porous plate to allow the last traces of benzene to evaporate. The yield of white crystals of homophthalic acid, melting at $180-181^{\circ}$ (Note 6), amounts to 67-77 g. (66-77% calculated on the basis of 90% indene content of the commercial indene).

B. *Homophthalic anhydride*. A mixture of 60 g. (0.33 mole) of dry homophthalic acid and 33.7 g. (31 ml., 0.33 mole) of acetic anhydride in a 200-ml. round-bottomed flask fitted to a reflux condenser by a ground-glass joint is refluxed for 2 hours. The mixture is cooled to about 10° for 30 minutes, and the solid anhydride is collected on a Büchner funnel with the aid of suction. It is washed with 10 ml. of glacial acetic acid and pressed, and as much of the solvent as possible is removed by suction. The product is spread out on a porous plate for several hours

(Note 7); it amounts to 46–47.5 g. (85–88%) of white crystals melting at 140–141° (Note 8).

2. Notes

1. Indene of approximately 90% purity may be obtained from the Koppers Company, Pittsburgh, Pennsylvania, or United Gas Improvement Company, Philadelphia, Pennsylvania. The practical grade of the same purity from the Eastman Kodak Company may also be used. If the material is dark colored, it should be redistilled and the fraction boiling from 180° to 182° should be used.

2. It is important to control the temperature of this oxidation. If the oxidation is carried out at the reflux temperature,¹ the yield of purified acid drops to about 52–54%.

3. Homophthalic acid possesses an appreciable solubility in water (about 1.6 g. per 100 ml. at 20°), hence it is necessary to cool the solutions and wash liquids to obtain good yields.

4. This extraction removes about 7–8 g. of oily alkali-insoluble products.

5. This azeotropic distillation is the quickest method for drying homophthalic acid. The acid turns dark colored if dried in an oven at 110°. It may be dried over anhydrous calcium chloride in a vacuum desiccator for 24–36 hours; it melts at 180–181°.

6. The melting point depends on the rate of heating. When the melting-point tube was placed in the bath preheated to 170°, the acid melted at 180–181°. When the heating was started at room temperature, the observed melting point was 172–174°.

7. Drying in an oven causes some loss because the anhydride sublimes.

8. If all the acetic acid is not removed the product melts lower, *ca.* 138–139°

3. Methods of Preparation

In addition to the methods listed under the preparation from phthalide² via *o*-carboxyphenylacetonitrile, homophthalic

acid has been obtained by hydrolysis of *o*-cyanobenzyl cyanide;³ by oxidation of β -indanone with alkaline permanganate solution;⁴ from tetralin via phthalonic acid;⁵ and from α -indanone by chromic acid oxidation⁶ or by nitrosation, Beckmann rearrangement, and hydrolysis.⁷ The oxidation of indene by alkaline permanganate produces homophthalic acid⁸ and phthalic acid.⁹ The above procedure is a modification of that described by Meyer and Vittenet¹⁰ and by Whitmore and Cooney.¹

Homophthalic anhydride has been obtained by heating the acid alone,¹¹ and by refluxing with acetyl chloride¹² or with acetic anhydride.¹³

¹ Whitmore and Cooney, *J. Am. Chem. Soc.*, **66**, 1237 (1944).

² *Org. Syntheses*, **22**, 62 (1942).

³ Gabriel and Otto, *Ber.*, **20**, 2224, 2502 (1887).

⁴ Benedikt, *Ann.*, **275**, 354 (1893).

⁵ Davies and Poole, *J. Chem. Soc.*, **1928**, 1617.

⁶ Ingold and Piggott, *J. Chem. Soc.*, **123**, 1497 (1923).

⁷ Perkin and Robinson, *J. Chem. Soc.*, **91**, 1082 (1907).

⁸ Heusler and Schieffer, *Ber.*, **32**, 29 (1899).

⁹ Cooney, Ph. D. Thesis, Poly. Tech. Inst. Brooklyn, 1943.

¹⁰ Meyer and Vittenet, *Compt. rend.*, **194**, 1250 (1932); *Ann. chim.*, (10) **17**, 274 (1932).

¹¹ Gräbe and Trumphy, *Ber.*, **31**, 375 (1898).

¹² Wislicenus, *Ann.*, **233**, 108 (1886); Price, Lewis, and Meister, *J. Am. Chem. Soc.*, **61**, 2760 (1939).

¹³ Dieckmann, *Ber.*, **47**, 1432 (1914).

β -(2-HYDROXYETHYLMERCAPTO)PROPIONITRILE

(Propionitrile, β -(2-hydroxyethylmercapto)-)



Submitted by LEON L. GERSHBEIN and CHARLES D. HURD.

Checked by CLIFF S. HAMILTON and JOHN A. STEPHENS.

1. Procedure

In a 500-ml. three-necked round-bottomed flask equipped with sealed stirrer, a reflux condenser, a dropping funnel, and a thermometer is placed 78 g. (70 ml., 1 mole) of 2 mercaptoethanol (Note 1). Into the dropping funnel is poured 67 ml.

(54.3 g., 1 mole) of acrylonitrile (Note 2), and after the addition of about 3 ml. of the nitrile, with stirring, the contents are warmed with a water bath to about 35–40° for 5 minutes. The remainder of the acrylonitrile is then added dropwise during 10 minutes. The temperature soon mounts to about 65° and is kept between 55° and 60° by intermittent short cooling with water until it only slowly increases or remains stationary at 55–60° (Note 3). Forty milliliters of acrylonitrile is then added all at once, cooling being applied if necessary, and the contents are stirred for 16 hours at room temperature. The product is distilled from a 250-ml. Claisen flask after removal of excess acrylonitrile under reduced pressure. The yield of nitrile distilling at 178–180°/14 mm., n_D^{25} 1.5101, as a colorless viscous liquid is 121–123 g. (92–94%) (Note 4).

2. Notes

1. The 2-mercaptoethanol was obtained from Carbide and Carbon Chemicals Corporation.

2. Commercial acrylonitrile may be used without further purification.

3. This requires about 30 minutes. As an inhibition period generally occurs, care must be taken in the initiation of the reaction and subsequent moderation of the heat evolved, but this operation can easily be controlled.

4. In the presence of alcoholic sodium hydroxide, either 2-mercaptoethanol or β -(2-hydroxyethylmercapto)propionitrile is converted to the dicyanoethylated product, 4-oxa-7-thiadecanedinitrile, $\text{NCCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{SCH}_2\text{CH}_2\text{CN}$. This basic agent can also be applied to the general reaction of thiophenols or mercaptans with acrylonitrile.

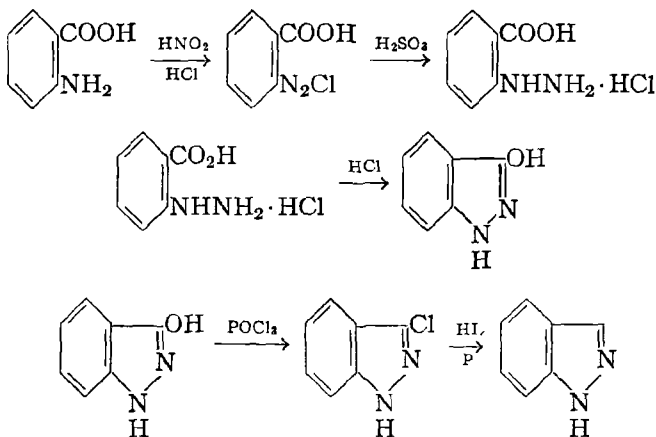
3. Methods of Preparation

This method is a modification of the directions of Hurd and Gershbain.¹ The compound has been made also² with piperidine as the basic catalyst.

¹ Hurd and Gershbain, *J. Am. Chem. Soc.*, **69**, 2331 (1947).

² Gillsbous, Miller, and O'Leary, *U. S. Pat. 2,397,960* [C.A., **40**, 3542 (1946)].

INDAZOLE



Submitted by EMILY F. M. STEPHENSON.

Checked by C. F. H. ALLEN, C. V. WILSON, and JEAN V. CRAWFORD.

1. Procedure

A. *o*-Hydrazinobenzoic acid hydrochloride. In a 2-l. beaker, provided with a stirrer and a low-temperature thermometer, and cooled in an ice-salt bath, are placed 42 g. (0.31 mole) of anthranilic acid and 300 ml. of water. The stirrer is started, and 340 ml. of concentrated hydrochloric acid (sp. gr. 1.18) is added in one portion; the anthranilic acid dissolves, and its hydrochloride begins to separate almost immediately. After the mixture has been cooled to 0°, a solution of 21.6 g. (0.31 mole) of technical sodium nitrite in 210 ml. of water is added from a dropping funnel, the tip of which extends below the surface of the suspension, at such a rate that the temperature never rises above 3°. The addition requires about 30 minutes; stirring is continued for 15 minutes longer, and at the end of this period a positive test with starch-iodide paper should be obtained (Note 1). The clear brown solution is then diluted with 150 ml. of ice water.

In a 12-l. flask, equipped with a low-temperature thermometer and surrounded by an ice-salt bath, a solution of sulfurous acid is prepared by saturating 2.4 l. of water at 0–5° with sulfur dioxide from a cylinder. A brisk stream of the gas is continued (Note 2) while the cold diazonium salt solution is added in about 150-ml. portions over a 30-minute period and the temperature is maintained at 5–10°; the reaction mixture assumes a dark orange color (Note 3). The cooling bath is removed, but sulfur dioxide is passed into the mixture for an additional half hour. After the mixture has been allowed to stand for 12 hours at room temperature, 3 l. of concentrated hydrochloric acid (sp. gr. 1.18) is added; the *o*-hydrazinobenzoic acid hydrochloride separates at once. The mixture is chilled to 0–5° and filtered through a pre-cooled Büchner funnel; the product is washed with two 50-ml. portions of ice-cold dilute (1 : 1) hydrochloric acid. The yield is 50–51 g. (86–88%); the salt melts at 194–195° with decomposition (Note 4) and is suitable for the next step without further purification (Note 5).

B. *Indazolone*. In a 2-l. round-bottomed flask to which a reflux condenser is attached are placed 47.1 g. (0.25 mole) of *o*-hydrazinobenzoic acid hydrochloride, 1.25 l. of water, and 12.5 ml. of concentrated hydrochloric acid (sp. gr. 1.18). The mixture is refluxed for 30 minutes. The resulting pale yellow solution is transferred in two portions to a 23-cm. evaporating dish and concentrated on the steam bath to about one-fourth its original volume. The indazolone separates at an early stage of the evaporation but redissolves as the concentration of acid increases. Sodium carbonate is added to the warm solution in small portions until the acid is neutralized (Note 6), and the suspension is allowed to stand for 2 hours. The nearly colorless indazolone is removed by filtration, washed with two 25-ml. portions of cold water, and air-dried. The yield of product, m.p. 246–249°, is 30–33 g. (90–98%) (Note 7).

C. *3-Chloroindazole*. In a 200-ml. flask connected by a glass joint to an air condenser protected by a drying tube are placed 26.8 g. (0.2 mole) of dry indazolone and 15.8 g. (16 ml., 0.2 mole) of dry pyridine (Note 8); 46.1 g. (27.6 ml., 0.3 mole) of phosphorus oxychloride is then added, with shaking, over a 10-minute

period. Heat is evolved, and acid fumes are generated. The mixture is heated with occasional shaking in an oil bath, which is maintained at 128–130° for 1 hour and at 130–140° for 4 hours. The clear brown solution is then cooled to 70° and poured, with hand stirring, upon 500 g. of cracked ice. This mixture is allowed to stand for 24 hours. The pale buff solid is removed, washed on the filter, first with 100 ml. of 0.5 *N* hydrochloric acid and then with 40 ml. of cold water, and air-dried (Note 9). The 3-chloro-indazole is crystallized from 3 l. of 20% ethanol. The yield is 21–22.5 g. (68–74%) of material melting at 148–148.5° (Note 10).

D. *Indazole*. In a 300-ml. flask are placed 15.3 g. (0.1 mole) of 3-chloroindazole, 18.6 g. (0.15 mole) of red phosphorus, and 100 ml. of constant-boiling hydriodic acid (sp. gr. 1.7) (Note 11). The mixture is refluxed for 24 hours (Note 12), cooled, and filtered through a sintered-glass funnel (Note 13) to remove the phosphorus; the flask and the solid are washed with two 20-ml. portions of water. The clear filtrate is transferred to a 300-ml. Claisen flask and concentrated to about 40 ml. by heating in a water bath at a reduced pressure. The residue is washed into a 250-ml. beaker with 70–80 ml. of hot water, and the clear solution is cooled in an ice bath and made strongly alkaline with concentrated ammonium hydroxide (about 80 ml. is required). The next day, the indazole is collected and dried; the white solid melts at 143–145° (Note 14).

The product is added to 75 ml. of benzene, and the suspension is boiled until the frothing has ceased, the benzene lost being replaced (Note 15); the resulting suspension is filtered to remove the insoluble material. The clear filtrate is heated to boiling, diluted with 25 ml. of petroleum ether (b.p. 70–90°), and allowed to cool slowly. The yield of white product, m.p. 145–146.5°, is 9.7–10.2 g. (82–86%). The over-all yield from anthranilic acid is 43–55%.

2. Notes

1. If the starch-iodide test is negative at this point a little solid sodium nitrite may be added.

2. This operation should be carried out in a hood or out-of-doors.

3. Small amounts of a red crystalline solid were obtained at this point by the checkers in several runs. This substance can be converted to *o*-hydrazinobenzoic acid by the addition of 5 ml. of concentrated hydrochloric acid to a suspension of 1 g. of the solid in 25 ml. of dilute (1 : 1) hydrochloric acid. The red solid changes to the white *o*-hydrazinobenzoic acid hydrochloride without apparent solution.

4. The melting point varies with the rate of heating. The values given were obtained with a bath preheated to 180°.

5. The free acid may be obtained by treatment of a solution of the hydrochloride with a concentrated aqueous solution of sodium acetate. The powdered hydrochloride (18.9 g., 0.1 mole) is dissolved in 567 ml. of water, and sodium acetate solution (8.2 g. [0.1 mole] of anhydrous sodium acetate in 30 ml. of water) is added. *o*-Hydrazinobenzoic acid separates at once; the mixture is chilled, and the light tan acid is removed by filtration, washed with two 25-ml. portions of water, and air-dried. The yield is 13.1 g. (86%); m.p. 248-250°. If a purer acid is required, the crude material may be recrystallized from ethanol (50 ml. per g.); the pale tan product then melts at 250-251.5°.

6. About 20 g. of sodium carbonate is required.

7. The indazolone may be purified further by recrystallization from methanol (24 ml. per g.), with filtration of the hot solution through a layer of Norite. It separates as white needles, m.p. 250-252°; the recovery is about 50%. An additional 10% of material (m.p. 246-248°) may be obtained by dilution of the filtrate with 2 volumes of water.

The submitter reports that the described method of purification gives a better product than is obtained by solution in dilute sodium hydroxide and reprecipitation with acid.

8. The submitter reports that dimethylaniline can be used but that it is less desirable because a small amount of a green by-product is formed.

9. The crude chloroindazole, m.p. 143-145°, is difficult to dry. Small quantities may be crystallized satisfactorily from water (250 ml. per g.). The submitter reports that a good product can be obtained by steam distillation but that even with superheated steam the distillation is very slow.

10. In a run 2.5 times this size, the checkers dissolved the crude product in 190 ml. of ethanol and diluted the hot filtrate with 260 ml. of water; the chloroindazole was obtained in 80% yield.

11. It is essential to use acid of this concentration.

12. This reaction time ensures complete conversion of the chloroindazole.

13. As an alternative procedure, the mixture may be diluted with 70 ml. of water and filtered through S & S No. 596 filter paper.

14. The crude indazole is so difficult to dry that the weight at this stage is not significant.

15. This operation is carried out in an open flask in the hood and at a point remote from flames; the indazole is dried by the steam distillation of the water with the benzene.

3. Methods of Preparation

The preparations of *o*-hydrazinobenzoic acid hydrochloride and indazolone are essentially those given by Pfannstiel and Janecke.¹ The procedure for the conversion of indazolone to indazole is a modification of that of Fischer and Seuffert.² A procedure involving the decarboxylation of indazole-3-carboxylic acid is described by Schad³ and by von Auwers.⁴

Indazole has been obtained in a variety of ways which are of no preparative value. The elimination of the amino group from aminoindazoles, first utilized by Witt,⁵ by the action of ethanol or sodium stannite on the diazonium compounds appears to be the only other useful procedure.

¹ Pfannstiel and Janecke, *Ber.*, **75**, 1104 (1942).

² Fischer and Seuffert, *Ber.*, **34**, 796 (1901).

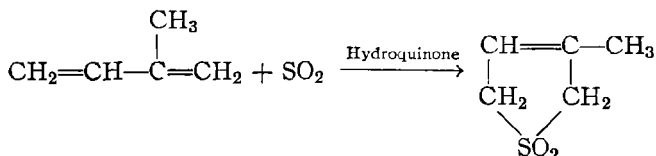
³ Schad, *Ber.*, **26**, 217 (1893).

⁴ von Auwers and Dereser, *Ber.*, **52**, 1344 (1919).

⁵ Witt, Nölting, and Grandmougin, *Ber.*, **23**, 3642 (1890).

ISOPRENE CYCLIC SULFONE

(Thiophene, 2,5-dihydro-3-methyl-, 1-dioxide)

Submitted by ROBERT L. FRANK and RAYMOND P. SEVEN.¹

Checked by A. E. BARKDOLL and R. S. SCHREIBER.

1. Procedure

Caution! If peroxides are present in the isoprene, they should be destroyed by washing with 10% acidified ferrous ammonium sulfate before distillation.

A 600-ml. steel reaction vessel (Note 1) is precooled before loading by filling it between one fourth and one half full of methanol and Dry Ice. After removal of the methanol and Dry Ice, the autoclave is charged with 120 g. (176 ml., 1.76 moles) of isoprene (Note 2), 113 g. (80 ml., 1.76 moles) of liquid sulfur dioxide, 88 ml. of methanol, and 4 g. of hydroquinone. The vessel is sealed, heated slowly to 85°, and maintained at that temperature for 4 hours. It is then cooled, the sulfone removed, the bomb rinsed with methanol, and the combined product and washings are treated hot with 5 g. of Norite. The filtered solution is concentrated to a volume of 250–300 ml., and the sulfone is allowed to crystallize. The material is filtered and washed with 50 ml. of cold methanol. Recrystallization from methanol (20 ml. per 25 g. of sulfone) yields 140–150 g. of thick, colorless plates. Concentration of the mother liquors raises the total yield to 182–191 g. (78–82%) (Note 3), melting at 63.5–64° (Note 4).

2. Notes

1. A steel reaction vessel of the type used for high-pressure catalytic hydrogenations is satisfactory. The pressure gener-

ated is less than 200 lb. For smaller quantities a heavy glass tube can also be used with proper precautions.

2. Commercial isoprene, obtained from Phillips Petroleum Company, should be freshly distilled before use, in order to eliminate isoprene dimers and polymers which are likely to accumulate in storage. If peroxides are present, they should be destroyed before distillation of the isoprene by washing with 10% acidified ferrous ammonium sulfate. As an added precaution, the distillation flask should not be permitted to go dry.

3. The yield of the cyclic sulfone depends upon the purity of isoprene. In one experiment, the checkers obtained the sulfone in 86% yield, using freshly distilled isoprene of 99 mole per cent purity, while the yield fell to 77% with commercial isoprene which had been distilled and stored at 5° for 1 week before use.

4. The checkers consistently obtained a slightly higher melting point (uncor.) in the range 64.4–65.4°. The purified cyclic sulfone serves as an ideal intermediate for the preparation of extremely pure isoprene, since the latter can be regenerated nearly quantitatively at 135–140°.² Other sulfones that can be prepared by this method and that are useful in the purification of dienes are those of butadiene, m.p. 65.5°,³ and 2,3-dimethylbutadiene, m.p. 135°.³ The sulfone of piperylene is a liquid.⁴

3. Methods of Preparation

Isoprene cyclic sulfone has been prepared only from isoprene and sulfur dioxide.²,³,⁵

¹ Work done under contract with the Office of Rubber Reserve, Reconstruction Finance Corporation.

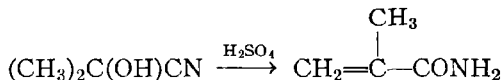
² Frank, Adams, Blegen, Deanin, and Smith, *Ind. Eng. Chem.*, **39**, 887 (1947).

³ Staudinger and Ritzenthaler, *Ber.*, **68**, 455 (1935).

⁴ Craig, *J. Am. Chem. Soc.*, **65**, 1006 (1943); Frank, Emmick, and Johnson, *J. Am. Chem. Soc.*, **69**, 2313 (1947).

⁵ Eigenberger, *J. prakt. Chem.*, (2) **127**, 307 (1930).

METHACRYLAMIDE



Submitted by RICHARD H. WILEY and WALTER E. WADDEY.

Checked by R. L. SHRINER and ARNE LANGSJOEN.

1. Procedure

In a 1-l. three-necked round-bottomed flask fitted with an efficient stirrer, a dropping funnel, and a thermometer, are placed 150 g. (82 ml., 1.5 moles) of 98% sulfuric acid (Note 1) and 1 g. of flowers of sulfur. To this is added, with rapid stirring, 85 g. (91 ml., 1 mole) of acetone cyanohydrin¹ (Note 2) over a period of 25 minutes, the temperature of the contents of the flask being kept at 75–80° by cooling in a water bath. At the end of this period, the water bath is replaced with an oil bath preheated to 160°. With continued stirring, the temperature of the reaction mixture is raised to 150° within 5 minutes and maintained at 150° for 15 minutes (Note 3). The reaction mixture is quickly cooled to room temperature by replacing the oil bath with an ice bath and is then poured into 300 ml. of cold water, and the flask is rinsed with 75 ml. of water. The diluted mixture is filtered (Note 4) through a 10-cm. Büchner funnel with the aid of suction. The filtrate is placed in a 1-l. beaker, cooled with an ice bath and 180–190 g. of anhydrous sodium carbonate sifted in with vigorous stirring (*Caution! foaming*) (Note 5). The precipitate is collected on a 20-cm. Büchner funnel and pressed and sucked as dry as possible. The crude product is dried in a vacuum desiccator over anhydrous calcium chloride for 36–48 hours (Note 6). The light cream- or tan-colored crude product weighs 300–400 g.

The crude dried solid is crushed to break up lumps and is placed in a 2-l. flask and heated and stirred mechanically with 500 ml. of boiling benzene. The solution is decanted, and the extraction is repeated four times using 200-ml. portions of

benzene. The combined benzene solutions are heated to boiling, treated with 2-4 g. of Norite, and filtered. On cooling, 48-52 g. of methacrylamide separates; m.p. 105-107° (Note 7). An additional 5-8 g., m.p. 103-105°, is obtained when the mother liquor is concentrated to 150 ml. and cooled. The yield of methacrylamide is 52-60 g. (61-70%) after storing in a vacuum desiccator over paraffin wax and anhydrous calcium chloride.

2. Notes

1. Acid of 98% strength may be prepared by the addition of 33.5 ml. of fuming sulfuric acid (15% SO₃) to 48 ml. of concentrated sulfuric acid of sp. gr. 1.84.

2. Acetone cyanohydrin of 98% purity may be purchased from the Rohm and Haas Company, Philadelphia, Pennsylvania.

3. This heating converts the intermediate compounds into methacrylamide sulfate. Longer periods of heating decrease the yield.

4. A small amount of dark polymeric material, which may form, is separated at this point.

5. Care is taken to crush lumps of sodium carbonate formed during the addition. The final reaction mixture should be slightly alkaline to litmus paper, and the temperature of the mixture should not rise above 25-30°.

6. The precipitated methacrylamide contains varying amounts of sodium sulfate. It is essential to obtain a dry product for the benzene extraction. The desiccator should be evacuated with an oil pump to about 5 mm. several times during 24-36 hours in order to obtain a sufficiently dry material.

7. The methacrylamide tends to retain some solvent. By placing the product in a vacuum desiccator containing paraffin wax shavings and anhydrous calcium chloride for 36-48 hours material with a melting point of 109-110° may be obtained.

3. Methods of Preparation

Methacrylamide has been prepared by the reaction of acetone cyanohydrin with concentrated sulfuric acid,^{2,3,4,5,6,7} and by

the hydrolysis of methacrylonitrile.⁸ The method described is an adaptation of that described by Crawford and McGrath.⁴

¹ *Org. Syntheses Coll. Vol. 2*, 7 (1943).

² Verhulst, *Bull. soc. chim. Belg.*, **30**, 563 (1930); **40**, 475 (1931).

³ Crawford, *J. Soc. Chem. Ind.*, **64**, 231 (1945).

⁴ Crawford and McGrath, U. S. pat. 2,140,469 [*C.A.*, **33**, 2536 (1939)]; Brit. pat. 440,967 [*C.A.*, **30**, 4180 (1936)].

⁵ Crawford and Grigor, U. S. pat. 2,101,822 [*C.A.*, **32**, 952 (1938)]; Brit. pat. 456,533 [*C.A.*, **31**, 2230 (1937)].

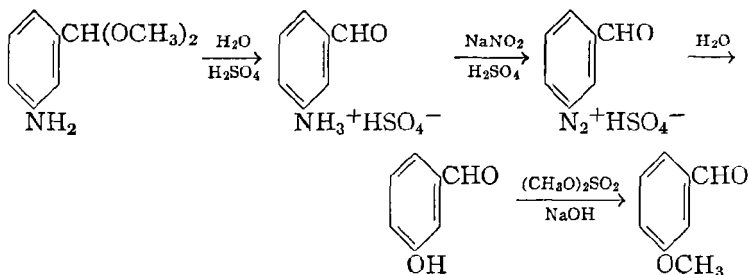
⁶ I. G. Farbenind. A.-G., Fr. pat. 813,844 [*C.A.*, **32**, 953 (1938)].

⁷ Rohm und Haas A.-G., Fr. pat. 815,908 [*C.A.*, **32**, 1816 (1938)].

⁸ Bruylants and Castille, *Bull. sci. acad. roy. Belg.*, **13**, 779 (1927); [*C.A.*, **22**, 2366 (1928)].

m-METHOXYBENZALDEHYDE

(Benzaldehyde, *m*-methoxy-)



Submitted by ROLAND N. ICKE, C. E. REDEMANN, BURNETT B. WISEGARVER, and GORDON A. ALLES.

Checked by H. R. SNYDER and FRANK X. WERBER.

1. Procedure

A. *m*-Hydroxybenzaldehyde. In a 2-l. three-necked flask, equipped with a mechanical stirrer, a thermometer, and a 250-ml. dropping funnel, 575 ml. of 6 *N* sulfuric acid is cooled to 0° by means of a salt-ice bath. The acid is stirred and maintained at 0° or below while 167 g. (1 mole) of *m*-aminobenzaldehyde dimethylacetal (p. 6) is added dropwise. The solution becomes

deep orange or red. When the addition of the amino compound is complete, a solution of 71 g. (1 mole) of 97% sodium nitrite in about 175 ml. of water is introduced slowly while the temperature of the acid solution is maintained at 5°. Stirring at 5° is continued for 1 hour to complete the reaction.

In each of two 4-l. beakers are placed 450 ml. of water and 50 ml. of concentrated sulfuric acid, and the solutions are heated to boiling with large burners. The cold diazonium solution is divided into two approximately equal portions which are placed in 500-ml. separatory funnels suspended above the beakers containing the boiling acid. The two portions of the diazonium solution are run dropwise into the strongly heated acid at such a rate that boiling continues. The solutions are boiled for 5 minutes after the additions are complete. They are then allowed to cool to room temperature and are finally stored overnight in a refrigerator. The crude product separates as a dark oil which crystallizes (Note 1) and becomes lighter in color upon standing. It is collected on a Büchner funnel and used in part *B* without purification (Note 2).

*Caution! The methylation should be carried out in a good hood. Methyl sulfate is quite toxic.*¹

B. m-Methoxybenzaldehyde. The crude *m*-hydroxybenzaldehyde is dissolved in about 550 ml. of 2 *N* sodium hydroxide in a 2-l. three-necked flask equipped with a mechanical stirrer, a thermometer, and a 125-ml. dropping funnel. The dark-colored solution is stirred while 126 g. (95 ml., 1 mole) of methyl sulfate (Note 3) is added dropwise and the temperature is maintained at 40–45°. When the addition is complete the mixture is stirred for 5 minutes. A 275-ml. portion of 2 *N* sodium hydroxide (Note 4) is added in one lot, and then 63 g. (47.5 ml.) of methyl sulfate is added as before, except that the temperature is allowed to rise to 50°. Stirring at 50° is continued for 30 minutes, the mixture is cooled, and the organic layer is extracted with ether (Note 5). The ether solution is dried over anhydrous sodium sulfate for 8 hours, then filtered and concentrated by distillation. The residue is distilled under reduced pressure. The yield of *m*-methoxybenzaldehyde, a pale yellow liquid boiling at 88–90°/3 mm., is 86–98 g. (63–72%) (Note 6).

2. Notes

1. Seeding the mixture helps to initiate crystallization.
2. If *m*-hydroxybenzaldehyde is desired, the crude product may be purified as described previously.²
3. A good technical grade of methyl sulfate was used.
4. The optimum amount of sodium hydroxide solution apparently varies according to the amount of acid remaining in the crude, wet hydroxybenzaldehyde employed in the methylation. The checkers found it advisable to increase the amount added at this point to 345 ml. It is wise to test the reaction mixture with litmus paper occasionally during the final heating period and to add alkali as necessary to keep the solution from becoming acid.
5. If the methylation is not complete, some *m*-hydroxybenzaldehyde will remain dissolved in the aqueous phase. This may be recovered by acidifying the alkaline solution and collecting any crystalline solid which separates.
6. As with other aromatic aldehydes, *m*-methoxybenzaldehyde is susceptible to air oxidation and should be stored in a bottle which will just hold the product, so that air space above the liquid is minimized.

3. Methods of Preparation

m-Methoxybenzaldehyde has been prepared by the reduction of *m*-methoxybenzoic acid,³ by the reaction of diazotized *m*-aminobenzaldehyde with methanol,⁴ by an acid hydrolysis of the phenylhydrazone which was obtained by oxidation of the hydrazine analog,⁵ and by the methylation of *m*-hydroxybenzaldehyde, with methyl iodide^{6, 7, 8, 9} and with methyl sulfate.^{4, 10}

¹ *Org. Syntheses*, **20**, 97 (1940).

² *Org. Syntheses*, **25**, 55 (1945).

³ Asano and Inuziwa, *J. Pharm. Soc. Japan*, **59**, 141 (1939)

⁴ Noeling, *Ann. chim.*, (8) **19**, 541 (1910).

⁵ Grammaticakis, *Compt. rend.*, **210**, 303 (1940).

⁶ Tiemann and Ludwig, *Ber.*, **15**, 2043 (1882).

⁷ Pschorr and Jaekel, *Ber.*, **33**, 1826 (1900).

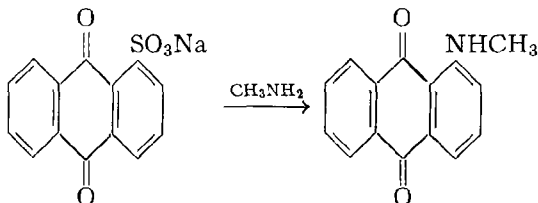
⁸ Staudinger and Kon, *Ann.*, **384**, 90 (1911).

⁹ Späth, *Monatsh.*, **34**, 1998 (1913).

¹⁰ Posner, *J. prakt. Chem.*, (2) **82**, 431 (1910).

1-METHYLAMINOANTHRAQUINONE

(Anthraquinone, 1-methylamino-)



Submitted by C. V. WILSON, J. B. DICKEY, and C. F. H. ALLEN.

Checked by GEORGE L. EVANS and R. S. SCHREIBER.

1. Procedure

A 1-gal. autoclave¹ (Note 1) is charged with 399 g. (1.29 moles) of technical sodium anthraquinone- α -sulfonate (Note 2), 45 g. (0.43 mole) of sodium chlorate, 780 g. (6.25 moles) of a 25% aqueous solution of methylamine, and 1.2 l. of water. The mixture is heated, with stirring, for 12 hours at 130–135° (Note 3). The heat is then shut off, but stirring is continued so that the product separates in an easily removable form. When cold, the autoclave is opened and the contents are removed; the material adhering to the walls is removed by water. The solid is filtered on a 13-cm. Büchner funnel. The red product is washed with two 500-ml. portions of hot water (70°) and dried in the air. The yield of 1-methylaminoanthraquinone, melting at 166–171° (Note 4), is 180–199 g. (59–65%) (Notes 5 and 6).

2. Notes

1. The shaking autoclave employed for high-pressure hydrogenations^{2,3} may be used equally well, but the quantities taken must be reduced to 155 g. (0.5 mole) of sodium anthraquinone-

α -sulfonate, 17.5 g. of sodium chlorate, 300 g. of a 25% aqueous methylamine solution, and 600 ml. of water. The checkers used a 2-gal. stirred autoclave (stainless steel).

2. A corresponding quantity of the potassium salt ⁴ can be utilized.

3. According to the checkers the heating time may be decreased to 8 hours if desirable.

4. The melting point varies slightly with the method of heating; if the bath is preheated to 160° before the sample is inserted, the melting point is 168–169.5°. When taken in the ordinary way, the melting point is 166–171°. This product is sufficiently pure for most purposes. One recrystallization from toluene raises the melting point 1°.

5. The yield depends upon the purity of the sodium anthraquinone- α -sulfonate. Apparent yields of as high as 87% have been obtained. The checkers employed technical grade material, which apparently resulted in an appreciable decrease in the yields of 76–80% reported by the submitters.

6. α -Chloroanthraquinone ⁵ can be used as a starting material. In this case, 433 g. (1.79 moles) are taken, together with 1.5 l. of pyridine, 600 ml. of 25% aqueous methylamine, and 2.5 g. of a copper salt. The product is washed with dilute (2%) hydrochloric acid. The yield is 380–400 g. (90–95%).

3. Methods of Preparation

1-Methylaminoanthraquinone has been prepared from 1-chloro-, 1-bromo-, and 1-nitroanthraquinone by treatment with alcoholic methylamine under pressure; ⁶ from 1-methoxy- and 1-phenoxyanthraquinone with methylamine in pyridine solution at 150°; ⁷ from potassium anthraquinone-1-sulfonate with aqueous methylamine at 150–160°; ^{8,9} from 1-aminoanthraquinone by treatment with formaldehyde, ¹⁰ or methyl alcohol ¹¹ in sulfuric acid or oleum; and by hydrolysis of *p*-toluenesulfonyl-methylaminoanthraquinone with sulfuric acid. ¹²

¹ *Org. Syntheses*, **22**, 20 (1942).

² American Instrument Company, Silver Spring, Maryland.

³ Parr Instrument Company, Moline, Illinois.

⁴ *Org. Syntheses* Coll. Vol. **2**, 539 (1943).

⁵ *Org. Syntheses* Coll. Vol. **2**, 128 (1943).

⁶ Ger. pat. 144,634 [*Frdl.*, **7**, 201 (1902-1904)].

⁷ Ger. pat. 165,728 [*Frdl.*, **8**, 289 (1905-1907)].

⁸ Ger. pat. 175,024 [*Frdl.*, **8**, 283 (1905-1907)].

⁹ Ger. pat. 256,515 [*Frdl.*, **11**, 551 (1912-1914)].

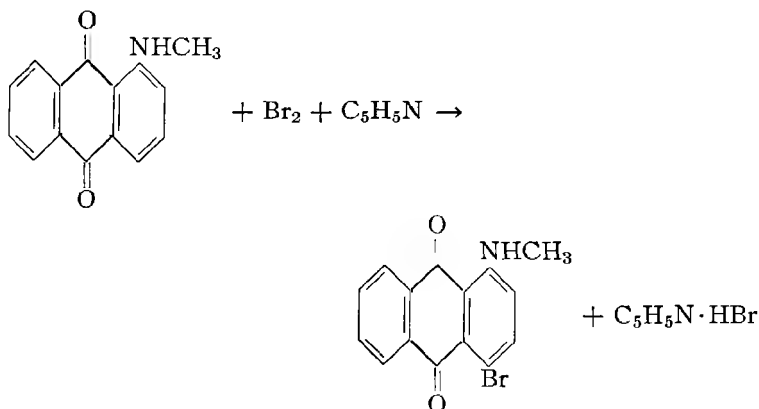
¹⁰ Ger. pat. 156,056 [*Frdl.*, **8**, 288 (1905-1907)].

¹¹ Ger. pat. 288,825 [*Frdl.*, **12**, 414 (1914-1916)].

¹² Ullmann and Fodor, *Ann.*, **380**, 320 (1911).

1-METHYLAMINO-4-BROMOANTHRAQUINONE

(Anthraquinone, 1-methylamino-4-bromo-)



Submitted by C. V. WILSON.

Checked by G. L. EVANS and R. S. SCHREIBER.

1. Procedure

In a 2-l. three-necked flask having ground-glass joints and equipped with a mechanical stirrer, a condenser (Note 1), and a dropping funnel are placed 119 g. (0.5 mole) of 1-methylaminoanthraquinone (p. 66) and 600 ml. of pyridine (Notes 2 and 3). The stirrer is started, and 90 g. (29 ml., 0.56 mole) of bromine is added over a period of 9-10 minutes. The flask and contents are now heated on the steam bath for 6 hours

with continuous stirring. At the end of this period the hot mixture is transferred from the flask to a beaker and allowed to cool. The solid that separates (Note 4) is collected on a Büchner funnel and is washed thoroughly with hot water to remove a considerable portion of pyridine hydrobromide which is precipitated along with the desired product. The resulting deep red 1-methylamino-4 bromoanthroquinone, after thorough drying, weighs 111–117 g. (70–74%). It melts at 193–195° and is pure enough for most purposes (Note 5).

2. Notes

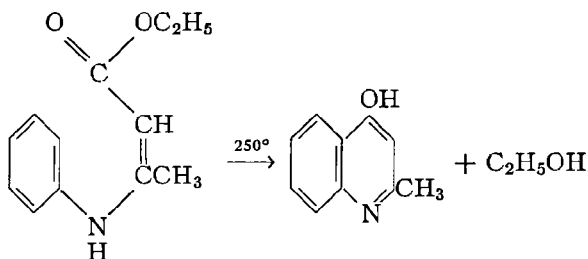
1. An air condenser of any type is sufficient.
2. A good grade of pyridine is essential. Very poor results are obtained with the practical or technical grades.
3. Larger volumes of pyridine have been used, but the yield drops progressively with increasing amounts.
4. Some of the solid separates during the heating on the steam bath.
5. It may be recrystallized, if desired, from pyridine, by the use of 3.5 ml. per g.; the melting point is raised to 195–196°.

3. Methods of Preparation

4-Bromo-1-methylaminoanthraquinone has been prepared from 4-bromo-1-nitroanthraquinone and methylamine at 60°,¹ and from 1-methylaminoanthraquinone in pyridine solution by treatment with two moles of bromine.² This procedure is based on the latter method.

¹ Ger. pat. 144,634 [*Frdl.*, 7, 201 (1902–1904)].

² Ger. pat. 164,791 [*Frdl.*, 8, 280 (1905–1907)].

2-METHYL-4-HYDROXYQUINOLINE**(4-Quinolinol, 2-methyl-)**

Submitted by GEORGE A. REYNOLDS and CHARLES R. HAUSER.

Checked by ARTHUR C. COPE and WILLIAM R. ARMSTRONG.

1. Procedure

In a 500-ml. three-necked round-bottomed flask equipped with a dropping funnel, a sealed mechanical stirrer, and an air condenser is placed 150 ml. of Dowtherm (Note 1). The Dowtherm is stirred and heated at the reflux temperature while 65 g. (0.32 mole) of ethyl β -anilinocrotonate (p. 42) is added rapidly through the dropping funnel. Stirring and refluxing are continued for 10–15 minutes after the addition is completed. The ethyl alcohol formed in the condensation reaction may be allowed to escape from the condenser through a tube leading to a drain, or it may be collected by attaching a water-cooled condenser set for distillation to the top of the air condenser. The mixture is allowed to cool to room temperature, at which stage a yellow solid separates. Approximately 200 ml. of petroleum ether (b.p. 60–70°) is added; the solid is collected on a Büchner funnel and washed with 100 ml. of petroleum ether (b.p. 60–70°). After air drying, the crude product is treated with 10 g. of Darco or Norite in 1 l. of boiling water (Note 2). The hot solution is filtered and allowed to cool. The white, hairlike needles of

2-methyl-4-hydroxyquinoline are separated by filtration. The yield of product, melting at 235–236° (cor.), is 43–46 g. (85–90%).

2. Notes

1. Dowtherm is a mixture of diphenyl and diphenyl ether, obtainable from the Dow Chemical Co.

2. If the treatment with decolorizing carbon is omitted, the product has a low melting point after several crystallizations.

3. Methods of Preparation

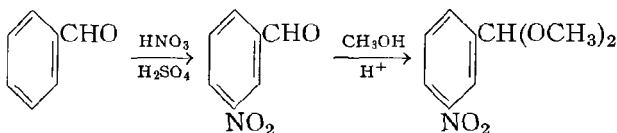
The present procedure is a modification of preparations described previously.^{1,2,3} The cyclization has been effected by allowing a solution of ethyl β -anilinocrotonate in concentrated sulfuric acid to stand at room temperature for several hours; by rapidly heating the ester to 240–250° without a solvent;² or by adding the ester to mineral oil at 250°.³ The procedure described has been applied to the preparation of other 2-substituted 4-hydroxyquinoline derivatives.⁴

¹ Knorr, *Ber.*, **16**, 2593 (1883).

² Conrad and Limpach, *Ber.*, **20**, 944 (1887).

³ Cavalito and Haskell, *J. Am. Chem. Soc.*, **33**, 1166 (1944).

⁴ Hauser and Reynolds, *J. Am. Chem. Soc.*, **70**, 2402 (1948).

***m*-NITROBENZALDEHYDE DIMETHYLACETAL**(Benzaldehyde, *m*-nitro-, dimethylacetal)

Submitted by ROLAND N. ICKE, C. E. REDEMANN, BURNETT B. WISEGARVER, and GORDON A. ALLES.

Checked by H. R. SNYDER and FRANK X. WERBER.

1. Procedure

A. *m*-Nitrobenzaldehyde. In a 3-l. three-necked flask provided with a dropping funnel, a thermometer, and an efficient mechanical stirrer is placed 1.25 l. of technical concentrated sulfuric acid (sp. gr. 1.84). The acid is stirred during the fairly rapid addition of 167 ml. (250 g., 4 moles) of technical fuming nitric acid (sp. gr. 1.49–1.50), with sufficient cooling by an ice bath so that the temperature of the mixed acids does not exceed 10°. The mixture is maintained at 5–10° while 213 g. (2 moles) of U.S.P. benzaldehyde (Note 1) is added with good stirring over a period of 2–3 hours. At the end of the addition the ice bath is removed and the mixture is allowed to stand overnight at room temperature.

The mixture is poured carefully onto about 3.25 kg. of cracked ice in a 2-gal. crock (Note 2) with manual stirring. The yellow precipitate is collected on a large Büchner funnel, washed with cold water, and pressed as dry as possible (Note 3). Further removal of water is accomplished by dissolving the moist product in about 100 ml. of warm benzene and separating the water layer in a separatory funnel. The benzene solution is filtered (Note 4) into a 1-l. distilling flask and concentrated on a steam bath. Distillation is discontinued when benzene no longer comes over or when nitrous fumes (from incompletely removed

nitric acid) appear. The residual *m*-nitrobenzaldehyde is sufficiently pure for use in the next step (Note 5).

B. *m*-Nitrobenzaldehyde dimethylacetal. The above crude product is dissolved in 750 ml. of technical anhydrous methanol, 1 ml. of concentrated hydrochloric acid is added if necessary (Note 6), and the solution is allowed to stand at room temperature for 5 days (Note 7). A solution of sodium methoxide in methanol is added until the solution is just alkaline to moistened litmus paper. The methanol is removed by distillation on a steam bath; the residue is cooled to room temperature and treated with cool water to dissolve the inorganic salts. The aqueous solution is extracted with two 50-ml. portions of ether, and the extracts are added to the crude acetal. The solution is subjected to a preliminary drying over anhydrous magnesium sulfate (or sodium sulfate), filtered, and then dried for at least 12 hours over anhydrous sodium carbonate. After the ether has been removed by distillation on a steam bath the residue is distilled under reduced pressure from a 500-ml. Claisen flask. The yield of the light yellow liquid acetal, boiling at 141–143°/8 mm. (Note 8), is 300–335 g. (76–85%) (Note 9).

2. Notes

1. Commercial benzaldehyde may contain some benzoic acid. When taken from a previously unopened bottle, U.S.P. benzaldehyde usually is quite satisfactory. If there is any doubt concerning its purity, the aldehyde may be washed with dilute sodium carbonate solution, dried over anhydrous sodium carbonate, and distilled under diminished pressure just before use.

2. Two 4-l. beakers may be used.

3. A small amount of an oily liquid passes through the filter; this material is a mixture of the *ortho* and *meta* isomers. If a very pure product is desired, this oil may be discarded, although some of the *meta* isomer will be lost. It is usually satisfactory to combine it with the solid material, the *m*-nitro acetal being obtained in a state of purity sufficient for most purposes in the final distillation.

4. A small amount of a solid by-product is removed.

5. If pure *m*-nitrobenzaldehyde is desired the benzene solution, diluted with more of the solvent, is washed with aqueous bicarbonate solution until the washings are alkaline to litmus paper, and thoroughly dried over anhydrous sodium sulfate. The solvent is removed, and the aldehyde is distilled under reduced pressure from a Claisen flask connected to an air-cooled condenser. The yield of material boiling at 119–123°/4 mm. is 226–254 g. (75–84%). The product readily crystallizes in the receiver.

6. When nitrous fumes are observed, there usually is enough acid present to catalyze the acetal formation.

7. The yield is not increased by extending the reaction period beyond 5 days.

8. The acetal boils at 116–119°/1 mm., 122–126°/2 mm., 130–132°/3 mm. The boiling range depends somewhat upon the rate of distillation.

9. The submitters obtained yields in the upper part of this range from runs twice the size described. They have stored samples of the product for as long as 4 years without deterioration.

3. Methods of Preparation

The only satisfactory method for the preparation of *m*-nitrobenzaldehyde is the direct nitration of benzaldehyde with a mixture of nitric and sulfuric acids. The procedure described is essentially that of Baker and Moffitt.¹

m-Nitrobenzaldehyde dimethylacetal has been prepared from the aldehyde and methanol in the presence of formiminomethyl ether hydrochloride² or Twitchell's reagent³ as the acid catalyst.

¹ Baker and Moffitt, *J. Chem. Soc.*, **1931**, 314.

² Claisen, *Ber.*, **31**, 1016 (1898).

³ Zaganianis, *Ber.*, **71**, 2002 (1938).

7. The submitter states that a number of aromatic mono- and dinitriles have been prepared by this procedure with slight or no modification in the temperature. The reaction mixtures were usually worked up by the acetone-ammonia method described in Note 6. Among the compounds prepared by this method are *o*-nitrobenzonitrile, *o*-bromobenzonitrile, *m*-methoxybenzonitrile, 4,4'-dicyanodiphenylsulfone, 4,4'-dicyanostilbene, α,γ -di-(4-cyanophenoxy)propane. With the last, a temperature of 185–190° for 20 minutes gave the best results. The yields before purification ranged between 75% and 95% and after purification between 63% and 79%. Aliphatic acids give low yields of the corresponding nitriles and, in some cases, chlorinated by-products.

3. Methods of Preparation

p-Nitrobenzonitrile has been prepared by the action of phosphorus pentoxide on *p*-nitrobenzamide,^{1,2} by the Sandmeyer reaction on *p*-nitroaniline,^{3,4} by thermal decomposition of *p*-nitrophenylglyoxylic acid oxime,⁵ by the thermal decomposition of *o*-benzoyl-*p*-nitrobenzaldoxime,⁶ by the action of acetic anhydride and phosphorus pentoxide on *p*-nitrobenzaldoxime,⁷ by the action of fused sodium chloride-aluminum chloride on *p*-nitrobenzamide,⁸ and by the action of tertiary amines on *syn-p*-nitrobenzaldoxime benzoate.^{9,10}

¹ Engley, *Ann.*, **149**, 298 (1869).

² Fricke, *Ber.*, **7**, 1321 (1874).

³ Sandmeyer, *Ber.*, **18**, 1492 (1885).

⁴ Bogert and Kohnstamm, *J. Am. Chem. Soc.*, **25**, 479 (1903).

⁵ Borsche, *Ber.*, **42**, 3597 (1909).

⁶ Neber, Hartung, and Ruopp, *Ber.*, **58B**, 1234 (1925).

⁷ Bogoslovskii, *J. Gen. Chem. U.S.S.R.*, **8**, 1784 (1938) [*C.A.*, **33**, 4973 (1939)].

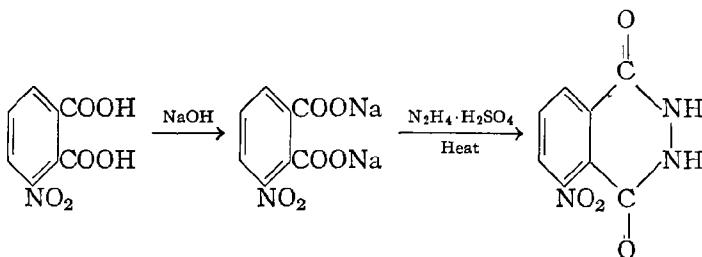
⁸ Norris and Klemka, *J. Am. Chem. Soc.*, **62**, 1432 (1940).

⁹ Hauser and Vermillion, *J. Am. Chem. Soc.*, **63**, 1224 (1941).

¹⁰ Vermillion and Hauser, *J. Am. Chem. Soc.*, **63**, 1227 (1941).

5-NITRO-2,3-DIHYDRO-1,4-PHTHALAZINEDIONE

(1,4-Phthalazinedione, 5-nitro-2,3-dihydro-)



Submitted by CARL T. REDEMANN and C. ERNST REDEMANN.

Checked by CLIFF S. HAMILTON and CARL L. CARLSON.

1. Procedure

In a 16-cm. evaporating dish are placed 42.2 g. (0.2 mole) of 3-nitrophthalic acid,¹ 50 ml. of water, and a few drops of phenolphthalein indicator solution. The mixture is made faintly alkaline to phenolphthalein with about 66 ml. (0.4 mole) of 6 *N* sodium hydroxide solution (Note 1), the last portions of which are added slowly with good stirring so that the end point may be observed. The color of the phenolphthalein is discharged by the addition of 0.2–0.3 g. of the 3-nitrophthalic acid, and 26.0 g. (0.2 mole) of hydrazine sulfate² is added. The solution is evaporated to dryness over a sand bath, with stirring at the latter part of the evaporation (Note 2), and the residual solid is cooled, ground in a mortar to a fine powder, and placed in a 200-ml. conical flask with 25 ml. of tetralin (Note 3). The mixture is heated at 160–170° for 3 hours and allowed to cool. After the addition of 50 ml. of benzene the solid is collected on a Büchner funnel and pressed down well, and most of the benzene is removed by suction. The solid is then washed with two 25-ml. portions of ether and allowed to stand in the air until the odor of ether is no longer detectable. The resulting material, weight 62.68 g., is an equimolar mixture of sodium sulfate and

5-nitro-2,3-dihydro-1,4-phthalazinedione, and it may be used directly for preparing 5-amino-2,3-dihydro-1,4-phthalazinedione (luminol, p. 8).

For purification, the crude material is suspended in 600–700 ml. of boiling water, and solid sodium carbonate is added in portions until the nitro compound has dissolved. Decolorizing carbon is added cautiously, and the suspension is boiled for a few minutes and filtered. The clear red-brown filtrate is acidified with concentrated hydrochloric acid, and the 5-nitro-2,3-dihydro-1,4-phthalazinedione is precipitated as a cream-colored flocculent solid. The solution is allowed to cool to room temperature, and the solid is separated by filtration and dried. The product thus obtained weighs 31–32 g. (75–78%) and has a melting point of 315–316° (dec.) when determined with the Kullman copper block (Note 4).

2. Notes

1. The strength of the sodium hydroxide solution is not critical; the equivalent amount of a solution of a different concentration may be used.

2. It is wise to cover the hand with a cloth or a glove while stirring, for the hot mixture may spatter if the heating is too rapid. The evaporation may be finished by transferring the evaporating dish to an oven shortly after the solid begins to separate. It is necessary to continue the evaporation until the solid is completely dry.

3. In an optional procedure the dry powder is heated in an oven at 160–170° for 3 hours.

4. No satisfactory solvent has been found for the recrystallization of 5-nitro-2,3-dihydro-1,4-phthalazinedione, but this precipitation gives a satisfactory product, free of sodium sulfate. The melting points given in the literature range from 297° to 320°.

3. Methods of Preparation

5-Nitro-2,3-dihydro-1,4-phthalazinedione has been prepared by heating 3-nitrophthalic acid with a large excess of hydrazine hydrate,³ by heating 3-nitrophthalic acid with hydrazine sulfate⁴

and sodium acetate, and by heating the nitro acid with hydrazine hydrate in alcohol at 150°. ⁵

¹ *Org. Syntheses* Coll. Vol. 1, 408 (1941).

² *Org. Syntheses* Coll. Vol. 1, 309 (1941).

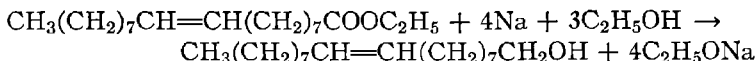
³ Bogert and Boroschek, *J. Am. Chem. Soc.*, **23**, 740 (1901).

⁴ Huntress, Stanley, and Parker, *J. Am. Chem. Soc.*, **56**, 241 (1934).

⁵ Rădulescu and Alexa, *Z. physik. Chem.*, **B8**, 393 (1930).

OLEYL ALCOHOL

(9-Octadecen-1-ol)



Submitted by HOMER ADKINS and R. H. GILLESPIE.

Checked by CLIFF S. HAMILTON, C. W. WINTER, and ALFRED STEPAN.

1. Procedure

In a 5-l. round-bottomed flask fitted with a large-bore reflux condenser are placed 200 g. (230 ml., 0.65 mole) of ethyl oleate (Note 1) and 1.5 l. of absolute ethanol (Note 2). Through the reflux condenser is added 80 g. (3.5 gram atoms) of sodium rapidly enough to keep up a vigorous reaction. The flask is shaken occasionally. After the initial reaction has subsided, about 200 ml. more of absolute alcohol is added, and the mixture is heated on a steam bath until all the sodium has reacted. Then 500 ml. of water is added, and the mixture is refluxed for 1 hour to saponify the unreacted ester. The mixture is cooled, and 1.2 l. of water is added. The unsaponifiable fraction is extracted with ether, and the extracts are washed with 1% potassium hydroxide solution and then with water till free of alkali when tested externally with phenolphthalein. The ether extract is dried over sodium sulfate, the ether removed by distillation, and the residue distilled through an efficient column (Note 3). A yield of 84–89 g. (49–51%), b.p. 150–152°/1 mm., is obtained.

Fifty grams of the crude oleyl alcohol is crystallized from 400 ml. of acetone at –20° to –25° (Note 4) in a jacketed sintered-

glass funnel (Note 5). The residue, amounting to about 25 g., is then recrystallized from 250 ml. of acetone at -5° (Note 6) to remove saturated alcohols. The oleyl alcohol in the filtrate is recrystallized at -60° to -65° (Note 7) and then distilled from a 25-ml. flask with a thermometer well and a low side arm. The yield is 13–16 g., b.p. $148\text{--}150^{\circ}$ /less than 1 mm.; n_D^{25} 1.4590.

2. Notes

1. The ethyl oleate used by the submitters was prepared by esterification of commercial U.S.P. grade oleic acid and fractionated through a Widmer column. The fraction boiling at $160\text{--}170^{\circ}/1$ mm., n_D^{25} 1.4482–1.4570, iodine value 83.6 (calculated 81.8), was used. The checkers distilled ethyl oleate (technical, Eastman Kodak Company) and used the fraction boiling at $164\text{--}166^{\circ}/1$ mm., n_D^{25} 1.4522.

2. The purity of the absolute alcohol is of prime importance. Alcohol dried only by a lime process gives a low yield (20–25%). The alcohol used in this procedure was dried over lime and then over aluminum *tert.*-butoxide, after which it was distilled directly into the flask used for the reaction.

3. The submitters used a modified Widmer column; the checkers, a Claisen flask modified with a short Vigreux column.

4. The temperature is controlled by selecting a liquid whose freezing point is approximately the temperature at which one wishes to carry out the crystallization, and crushed Dry Ice is added with stirring to keep just a slush. There must be an intimate mixture of solid and liquid at all times. Carbon tetrachloride was used for temperatures of -20° to -25° .

5. The apparatus was as follows:

A 50-ml. Pyrex sintered-glass funnel, with a sealed-on extension tube, was jacketed with an inverted 500-ml. wide-mouth bottle with the bottom cut off and the edges ground smooth. The jacketed funnel was then placed in a 250-ml. suction flask, the side arm of which was connected to a three-way stopcock. One arm of the stopcock was connected to a water aspirator, the other to a large test tube ($1\frac{1}{8}$ in. by 8 in.) fitted with a two-hole stopper. From the second hole in this stopper was led a tube

extending to the bottom of a smaller test tube partly filled with mercury. During crystallization, this large test tube was filled three-quarters full of Dry Ice, the carbon dioxide gas evolved being allowed to bubble up through the bottom of the sintered-glass funnel. This prevents the solution from filtering through and also stirs the solution by the rise of small carbon dioxide bubbles, and hence induces crystallization. The porosity of the sintered-glass funnel is a factor in the size and number of bubbles formed. The mercury trap may be raised or lowered to adjust the pressure, and to act as a vent to prevent the accumulation of carbon dioxide to give excessive pressures. After crystallization had taken place (about 1 hour) the stopcock was turned to the aspirator and the solution immediately filtered. With this apparatus, about 80 ml. of solution may be crystallized at a time, and no transferring from one container to another is necessary. The checkers found it more convenient to use a 500-ml. sintered-glass funnel along with a proportionally larger bottle, flask, etc. The 400 ml. of acetone solution was then poured into the funnel in 50-ml. portions with adequate cooling intervals.

6. A crushed ice-salt bath was used.

7. A Dry Ice-chloroform bath was used.

3. Methods of Preparation

Oleyl alcohol has been prepared by the action of sodium and absolute alcohol on ethyl oleate,¹ by the action of sodium and absolute butyl alcohol on butyl oleate,² and by the action of sodium and absolute *tert.*-butyl alcohol on ethyl oleate.³ This procedure is essentially that of Kass and Burr,⁴ who prepared linoleyl alcohol. The purification step was derived from the low-temperature crystallization technique of Hartsuch.⁵

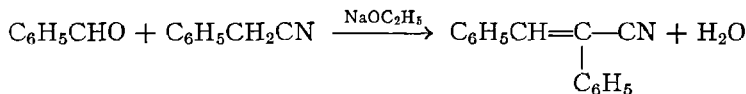
¹ Bouveault and Blanc, *Bull. soc. chim. France*, (3) **31**, 1210 (1904).

² *Org. Syntheses* Coll. Vol. **2**, 468 (1943).

³ Hausley, *Ind. Eng. Chem.*, **39**, 54 (1947).

⁴ Kass and Burr, *J. Am. Chem. Soc.*, **62**, 1796 (1940)

⁵ Hartsuch, *J. Am. Chem. Soc.*, **61**, 1142 (1939).

α -PHENYLCINNAMONITRILE(Acrylonitrile, α,β -diphenyl-)

Submitted by STANLEY WAWZONEK and EDWIN M. SMOLIN.

Checked by CLIFF S. HAMILTON and KARL W. R. JOHNSON.

1. Procedure

In a 2-l. beaker fitted with a strong, efficient, mechanical stirrer is placed a mixture of 106 g. (101 ml., 1 mole) of freshly distilled benzaldehyde and 117 g. (1 mole) of purified dry benzyl cyanide (Note 1), in 650 ml. of 95% ethanol (Note 2). To this mixture is added dropwise, with stirring, a solution of 7 g. of sodium ethoxide in 50 ml. of absolute ethanol (Note 3). When 40–50 ml. has been added, the mixture becomes warm, turns cloudy, and solidifies. Mechanical stirring is continued as long as possible, and then the mixture is stirred by hand with a thick stirring rod in order to break up the lumps that form. The mixture is cooled in an ice bath (Note 4), and the product is separated by filtration. The filtrate is removed and may be saved (Note 5). The white mass is washed first with 200 ml. of distilled water, then with 50 ml. of 95% ethanol to remove unchanged reagents. The nitrile is dried at 25° and melts at 86–88°. The yield is 178–199 g. (87–97%) of product sufficiently pure for most purposes. Recrystallization from 700 ml. of 95% ethanol gives 170–187 g. (83–91%) of a pure, white product melting at 88° (Note 6).

2. Notes

1. The benzyl cyanide may be purified by a procedure described earlier.¹ If commercial benzyl cyanide is used, the yield is between 80% and 90% of a slightly yellow product. Two recrystallizations are necessary for purification.

2. Denatured alcohol (Formula 3A) containing 10% absolute methanol is a satisfactory solvent for recrystallization.

3. A 40% solution of sodium hydroxide may also be used as the condensing agent; 35–60 ml. is required. With this reagent, the product is less pure and needs an additional recrystallization. The yields range from 70% to 82%.

4. This preliminary cooling helps to prevent clogging of the 20-cm. Büchner funnel used during filtration.

5. An additional 10–21 g. of crude nitrile melting at 84–86° can be obtained by evaporating the combined alcoholic filtrates to a volume of 300 ml. Two or three recrystallizations from 95% ethanol are necessary to raise the melting point to 88°.

6. Similar yields of substituted α -phenylcinnamonnitriles can be obtained using *p*-methoxybenzyl cyanide and anisaldehyde, or benzyl cyanide and anisaldehyde.^{2,3}

3. Methods of Preparation

α -Phenylcinnamonnitrile can be prepared from benzaldehyde and benzyl cyanide with no solvent and with sodium ethoxide as a catalyst.⁴ Sodium hydroxide⁵ (40%) or piperidine⁶ may also be used as catalysts. The nitrile has been made by the condensation of benzyl cyanide and excess benzyl chloride with strong sodium hydroxide at 170°^{7,8} and by heating α,β -diphenylsuccinonitrile with alcohol at 180° in a sealed tube⁹ or at 230–250° under 100–110 mm. pressure with palladium.¹⁰

This method is a modification of that of De Schutzenbach.⁴

¹ *Org. Syntheses* Coll. Vol. 1, 108 (1941).

² Wawzonek, *J. Am. Chem. Soc.*, **68**, 1157 (1946).

³ Niederl and Ziering, *J. Am. Chem. Soc.*, **64**, 885 (1942).

⁴ De Schutzenbach, *Ann. chim.*, (11) **6**, 90 (1936).

⁵ Walther, *J. prakt. Chem.*, (2) **53**, 454 (1896).

⁶ Knoevenagel, Ger. pat. 94,132 [*Chem. Zentr.*, **69**, 228 (1898)].

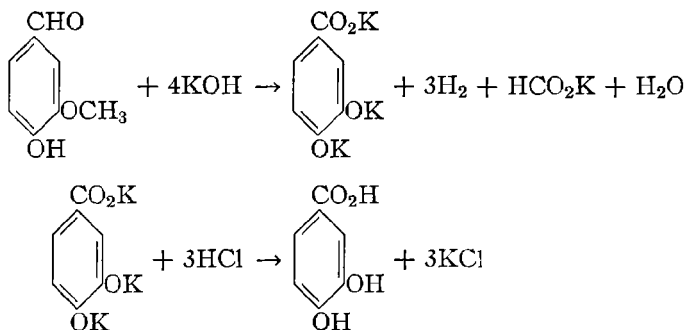
⁷ Neure, *Ann.*, **250**, 155 (1888).

⁸ Janssen, *Ann.*, **250**, 129 (1888).

⁹ Chalaney and Knoevenagel, *Ber.*, **25**, 297 (1892).

¹⁰ Knoevenagel and Bergdott, *Ber.*, **36**, 2861 (1903).

PROTocatechuic Acid
(Benzoic acid, 3,4-dihydroxy-)



Submitted by IRWIN A. PEARL.

Checked by C. F. H. ALLEN and CALVIN WOLF.

1. Procedure

In a stainless-steel beaker of approximately 3-l. volume (180 mm. by 150 mm.) (Note 1), equipped with an efficient mechanical stainless-steel stirrer and heated by an electric hot plate, are placed 84 g. (2 moles) of 97% sodium hydroxide pellets, 332 g. (5 moles) of 85% potassium hydroxide pellets (Note 2), and 50 ml. of water. The mixture is stirred and heated. When the temperature of the fluid mixture reaches 160°, 152 g. (1 mole) of vanillin is added in portions over a period of 2.5–3 minutes at a rate sufficient to maintain the reaction (Note 3). The temperature at this point is 190–195°. Stirring is continued and heat is applied until the temperature reaches 240–245° (Note 4). The temperature is maintained at 240–245° for 5 minutes. The hot plate is removed, and the mixture is allowed to cool with stirring. When the mixture has cooled to about 150–160°, 1 l. of water is added, and the mixture is stirred until all the fusion mixture is dissolved. The solution is transferred to a 4 l. beaker, another 500 ml. of water is added, and sulfur dioxide gas is introduced for 2 minutes (Note 5); the mixture is then completely acidified

with 1.5 l. of 6 *N* hydrochloric acid. The acidified mixture is cooled in an ice bath (5°) for 2 hours, and the crystalline precipitate is filtered, washed on the filter with two 100-ml. portions of ice water, and air dried. The tan crystals of protocatechuic acid melting at 196–198° weigh 90–100 g. Extraction of the filtrate and washings with two 1-l. portions of ether yields an additional 45–55 g. of protocatechuic acid melting at 190°. The total yield of crude protocatechuic acid amounts to 135–153 g. (89–99%) (Note 6).

2. Notes

1. In the checkers' opinion a 2-l. beaker is sufficiently large, and the contents are easier to stir. Iron or nickel pots have also been used.

2. The exact proportion of sodium hydroxide to potassium hydroxide is not too critical as long as the total amount of alkali is more than 7 moles. Mixtures containing from 10% to 60% sodium hydroxide become fluid between 120° and 130°. Increased percentages of sodium hydroxide in the mixture result in darker protocatechuic acid, but yields are not affected until 70% sodium hydroxide is reached.

3. This reaction is the oxidation of vanillin to vanillic acid with the liberation of hydrogen.

4. The demethylation of vanillic acid to protocatechuic acid takes place to a slight degree between 210° and 235° but goes to completion only at temperatures above 240–245°.

5. The sulfur dioxide treatment prevents the formation of a very dark-colored product when the reaction mixture is acidified with a strong acid.

6. The first crop of acid is a light tan and is suitable for most purposes. It can be improved slightly by recrystallizing from hot water, with 3 ml. per g. and 1 g. of Norite for every 10 g. of acid; the recovery is 75%, the remainder being retained by the charcoal. This recrystallized acid is a cream color and melts at 199–200°. If the Norite is omitted, the recovery is 90%, m.p. 198–199°, and color unchanged.

The second crop is of decidedly inferior quality. It is easily purified as follows: Fifteen grams of crude product is dissolved

in 100 ml. of 10% sodium hydroxide solution at room temperature, 2 g. of Norite is added, and the mixture is stirred for 10 minutes and filtered. Sulfur dioxide is then passed in for 2 minutes, after which 60 ml. of 6 *N* hydrochloric acid is added. After chilling and standing, 10 g. (67%) of purified protocatechuic acid, m.p. 196–198°, is recovered.

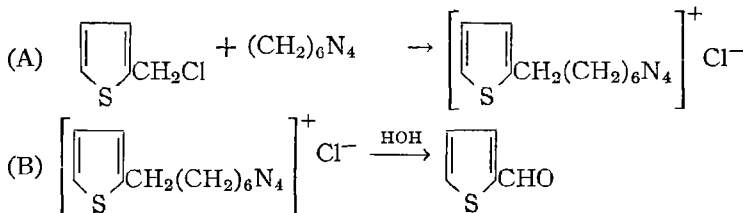
3. Methods of Preparation

The only practical method for the preparation of protocatechuic acid is by the alkaline fusion of vanillin.^{1,2}

¹ Pearl, *J. Am. Chem. Soc.*, **68**, 2180 (1946).

² Tiemann and Haarman, *Ber.*, **7**, 617 (1874).

2-THIOPHENEALDEHYDE



Submitted by KENNETH B. WIBERG.

Checked by CLIFF S. HAMILTON and J. L. PAULEY.

1. Procedure

A. 2-Thienylmethylhexamethylenetetrammonium chloride. In a 1-l. round-bottomed flask are placed 67 g. (0.5 mole) of 2-chloromethylthiophene (p. 31), 400 ml. of chloroform, and 70 g. (0.5 mole) of hexamethylenetetramine. The flask is fitted with a reflux condenser, and the mixture is boiled gently for 30 minutes. The mixture is cooled, and filtered on a Büchner funnel. The precipitate is washed with 100 ml. of cold chloroform, drained thoroughly, and air-dried. The yield is 128–136 g. (94–99%) of a white powder.

B. *2-Thiophenealdehyde*. The hexamethylenetetrammonium salt is placed in a 2-l. round-bottomed flask containing 400 ml. of warm water. The flask is fitted for steam distillation, and steam is passed in until all the aldehyde has distilled (Note 1). The distillate is cooled, 10 ml. of 6 *N* acetic acid is added (Note 2), and the aldehyde is extracted with two 100-ml. portions of ether. The ether solution is dried over anhydrous calcium chloride, and the ether is evaporated on a steam bath until the volume of the solution has decreased to about 50 ml. The solution is placed in a 100-ml. Claisen flask, the ether is removed by distillation, and the aldehyde distilling at 89–91°/21 mm., n_D^{25} 1.5880, is collected. The yield is 27–30 g. (48–53%) of a colorless oily liquid which darkens slowly on standing (Note 3).

2. Notes

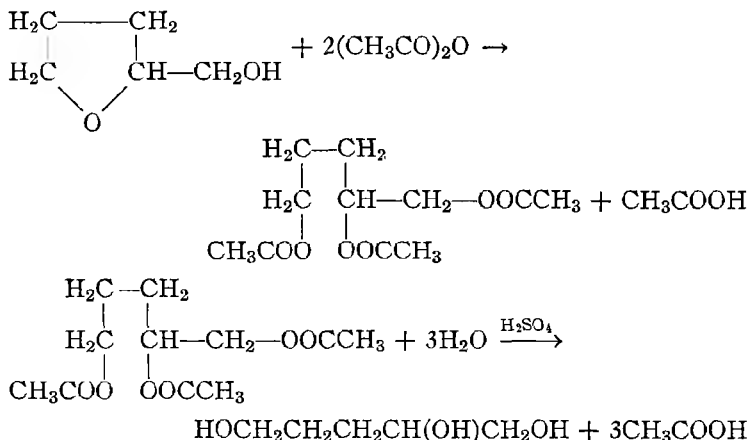
1. About 1.5 l. of distillate is collected before all the thiophenealdehyde is distilled over.

2. The acetic acid is added to remove traces of amines that come over in the steam distillation. This method of purification must be used because of the high solubility of the bisulfite addition compound of the aldehyde.

3. If the aldehyde is to be stored for any period of time, the addition of a small amount of hydroquinone is advisable.

3. Methods of Preparation

2-Thiophenealdehyde has been prepared by the decarboxylation of 2-thienylglyoxalic acid,¹ by the action of 2-thienylmagnesium iodide on ethyl orthoformate followed by hydrolysis of the acetal,² in small yields by the Rosenmund reduction of 2-thiophenecarboxylic acid chloride,³ in small yields by the action of hydrogen cyanide, hydrogen chloride, and aluminum chloride on thiophene using benzene as a solvent,⁴ by a series of reactions from 1-chloro-2,3-diketocyclopentane,⁵ by the hydrolysis of 2-thienylmethylhexamethylenetetrammonium chloride in neutral solution,⁶ and by the action of *N*-methylformanilide on thiophene in the presence of phosphorus oxychloride.⁷

¹ Biedermann, *Ber.*, **19**, 636 (1886).² Grischkewitch-Trochimowski, *J. Russ. Phys. Chem. Soc.*, **44**, 570 (1912).³ Barger and Easson, *J. Chem. Soc.*, **1938**, 2100.⁴ Reichstein, *Helv. Chim. Acta*, **13**, 349 (1930).⁵ Hantzsch, *Ber.*, **22**, 2838 (1889).⁶ Dumi, Waugh, and Dittmer, *J. Am. Chem. Soc.*, **68**, 2118 (1946).⁷ King and Nord, *J. Org. Chem.*, **13**, 635 (1948).**1,2,5-TRIHIDROXPENTANE****(1,2,5-Pentanetriol)**Submitted by OLIVER GRUMMITT, JAMES A. STEARNS, and
A. A. ARTERS.Checked by EUGENE DINEEN, CHRISTOPHER L. WILSON, and
CHARLES C. PRICE.**1. Procedure**

In a 5-l. three-necked flask fitted with a mercury-sealed mechanical stirrer, a 500-ml. dropping funnel, and an efficient reflux condenser are placed 2630 ml. (2856 g., 28 moles) of acetic anhydride and 57 g. of crushed anhydrous zinc chloride. This mixture is stirred and brought to gentle boiling. After 5-10 minutes at reflux, 680 ml. (714 g., 7 moles) of redistilled tetrahydrofurfuryl alcohol (Note 1) is added from the dropping funnel at such a rate

that the mixture refluxes vigorously. This addition requires about 30 minutes. The mixture is then stirred and refluxed gently for 24 hours. After being cooled, about one-half of the liquid is decanted from the zinc chloride residue through a glass wool plug in a funnel into a 2-l. Claisen flask and then distilled under reduced pressure. The second portion is likewise distilled. The total weight of fore-run is 1740–1780 g. (Note 2). The 1,2,5-triacetoxypentane is collected at 155–165°/14 mm. The yield is 1500–1550 g. (87–90%).

Fifteen hundred grams (6.1 moles) of the ester and 1.2 l. of 1% sulfuric acid (6.9 ml. of concentrated acid in 1.2 l. of solution) are added to a 5-l. round-bottomed flask fitted with a reflux condenser. The mixture is heated strongly and agitated by tilting the ring stand back and forth until the two layers become homogeneous. This initial hydrolysis step requires 15–30 minutes. When homogeneity is attained, the flask and condenser are set for steam distillation. The flask is heated by a Meker burner to maintain approximately constant volume, and the mixture is vigorously steam-distilled until 20 l. of distillate has been collected (Note 3). The residue is allowed to cool and then made basic to litmus paper by the addition of 10–20 g. of lime in small portions with vigorous agitation. The calcium sulfate is removed by suction filtration, the filtrate tested again with litmus paper to make certain that it is basic (Note 4), and the filtrate distilled under reduced pressure. This is most conveniently done by placing about one-half of the solution in a 2-l. Claisen flask, heating the flask in an oil bath at 100–110°, and distilling the water under the pressure of the water pump. The remainder of the filtrate is added, the water is removed, and the distillation is continued with an oil or mercury-vapor pump. The yield of 1,2,5-trihydroxypentane collected at 167–170°/0.5–1.0 mm. is 460–520 g. (63–71%); n_D^{25} 1.4730 (Note 5).

2. Notes

1. Tetrahydrofurfuryl alcohol from the Quaker Oats Company was redistilled, and the portion boiling at 175–177° was used. If the 1001 industrial grade of alcohol is used without

purification, the yield of triacetate is about 70% of the theoretical.

2. This consists mostly of acetic acid, acetic anhydride, and some tetrahydrofurfuryl acetate. By fractional distillation through a 15-in. glass-helix-packed column, $\frac{1}{2}$ in. in diameter, about 700 g. of acetic acid boiling at 117–125° and about 1075 g. of acetic anhydride boiling at 137–142° can be recovered.

3. With 10-mm. glass tubing for the steam inlet and outlet and an efficient condenser the maximum rate of steam distillation is 3 l. per hour. The 20 l. of distillate collected contains 95% of the calculated yield of acetic acid. The removal of the acetic acid is slow because the rate of hydrolysis in the final stages appears to be slow and the rate of acetic acid distillation is slow. The remainder of the acid is collected so slowly that it is not considered worth while to distil further, although the yield of product can be slightly increased.

4. If an acidic solution is distilled, the yield of product is decreased, probably because of dehydration and etherification reactions.

5. Analysis of this product for hydroxyl group content by the acetic anhydride-pyridine method gave 40.0%, compared to a calculated value of 42.5%, indicating a purity of 94%.

3. Methods of Preparation

1,2,5-Trihydroxypentane has been made by saponification of 1,2,5-triacetoxypentane with barium hydroxide^{1,2} and by hydrolysis with 0.1 *N* hydrochloric acid.³ The triacetoxypentane has been made by the action of potassium acetate and acetic anhydride on 4,5-dibromopentanol-1¹ or 1,2,5-tribromopentane^{2,4} or 1-chloro-4,5-diacetoxypentane,⁵ but it is most conveniently made by the reaction of acetic anhydride with tetrahydrofurfuryl alcohol.^{3,4} The present method is a modification of that described by Wilson.³

¹ Paul, *Compt. rend.*, **192**, 1574 (1931).

² Paul, *Ann. chim.*, (10) **18**, 303 (1932).

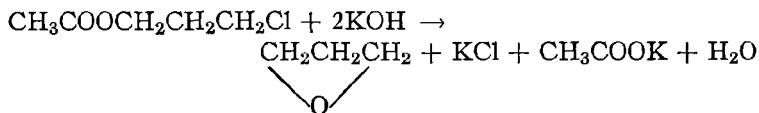
³ Wilson, *J. Chem. Soc.*, **1945**, 48.

⁴ Paul, *Bull. soc. chim. France*, **53**, 417 (1933).

⁵ Paul, *Compt. rend.*, **211**, 645 (1940).

TRIMETHYLENE OXIDE

(Oxetane)



Submitted by C. R. NOLLER.

Checked by C. F. H. ALLEN and F. W. SPANGLER.

1. Procedure

A 3-l. Pyrex flask (Note 1) is fitted with an efficient mechanical stirrer, a dropping funnel, a thermometer, and an upright tube (Note 2) to act as an air condenser and to carry the trimethylene oxide vapors through a spiral condenser. In the flask are placed 1344 g. (24 moles) of potassium hydroxide and 120 ml. of water. The contents are heated to about 140° with stirring (Note 3). The upper part of the flask should be kept sufficiently hot so that the potassium hydroxide mush which is thrown up on the sides does not solidify. The spiral condenser is then packed with an ice-salt mixture, and 1092 g. (8 moles) of γ -chloropropyl acetate (p. 33) (Note 4) is slowly run into the flask by means of the dropping funnel so that the distillate comes over at the rate of about one drop a second. The time required for the addition is 1.5–3 hours. After all the ester had been added, the mixture is stirred, with continued heating at 140–150°, until the distillate amounts to 250–400 g., depending on how efficiently the air condenser has separated the trimethylene oxide from higher-boiling substances. About 100 g. of potassium hydroxide pellets is added to the crude distillate, which is then distilled through a 25-cm. fractionating column packed with $\frac{1}{4}$ -in. Berl Saddles. By careful distillation the trimethylene oxide can be obtained in a single fractionation, the portion boiling at 45–50° being collected. The higher-boiling residue still contains some trimethylene oxide, but consists mostly of water, allyl

alcohol, and unchanged γ -chloropropyl acetate. The yield is 195–205 g. (42–44%). Redistillation over freshly fused potassium hydroxide gives a product boiling at 47–48°; n_D^{23} 1.3905.

2. Notes

1. A half-gallon jacketed iron autoclave may be employed.
2. A plain 90-cm. 10-mm. tube or a 30-cm. Vigreux column is equally satisfactory.
3. An electric heating mantle is advisable. The reaction is exothermic, and if it appears to become too vigorous the current is temporarily discontinued.
4. The submitter states that a yield of 20–25% may be obtained when trimethylene chlorohydrin is substituted for the acetate, with two moles of potassium hydroxide and 10 ml. of water per mole of chlorohydrin.

3. Methods of Preparation

This procedure is an improvement upon that of Reboul,¹ and of Derick and Bissell.² Reboul, as also did Ipatow,³ used trimethylene chlorohydrin, but the yield is higher from the acetate.

¹ Reboul, *Ann. chim.*, (5) **14**, 495 (1878).

² Derick and Bissell, *J. Am. Chem. Soc.*, **38**, 2478 (1916).

³ Ipatow, *J. Russ. Phys. Chem. Soc.*, **46**, 67 (1914) [*C.A.*, **8**, 1965 (1914); *Chem. Zentr.*, **85**, I, 2161 (1914)].

SUBJECT INDEX

(This cumulative index comprises material from Volumes 20 through 29 of this series, for previous volumes see Collective Volumes 1 and 2)

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Preparations are listed under the names which are used commonly for the compounds. For the convenience of those who wish to make a complete survey of the literature on any preparation, the *Chemical Abstracts* indexing name for each compound is given as a subtitle when that name differs from the title of the preparation.

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Organic Syntheses invites the submission of preparations of compounds which are of general interest or which illustrate useful synthetic methods. Preparations are welcomed particularly from those who have had occasion to work out the optimum conditions of preparation. The directions should be written in the style employed in the latest volume of *Organic Syntheses*. A copy of the current style sheet will be sent to those who request it. Full details for all steps in the procedures should be included, and the range of yields should be reported rather than the maximum yield obtainable. Wherever possible the melting point, the boiling range at various pressures, and the refractive index of each product should be given. The method of preparation or source of compounds used should be recorded as well as criteria of purity. Two copies of the directions should be sent to the Secretary. Additions, corrections, and improvements to previously published preparations are likewise welcomed.

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